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Vol. XIX, No. 2 FEBRUARY, 1930

JOURNAL

MAR 3 1930

OF THE

AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 78th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN BALTIMORE, DURING WEEK OF MAY 5, 1930.

The 1930 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conferences of Pharmaceutical Association Secretaries and of Pharmaceutical Law Enforcement Officials will also be held at Baltimore, same time and place.

Local Secretary—Samuel Y. Harris, Lombard & Poppleton Sts., Baltimore, Md.

For Association Roster and Roster of the Boards of Pharmacy, of Officers of Pharmaceutical Associations, Local Branches, see pages x, xii, xiv, etc.

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INVITATION TO THE SEVENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION IN BALTIMORE, DURING THE WEEK OF MAY 5, 1930.

SAMUEL Y. HARRIS, LOCAL SECRETARY.

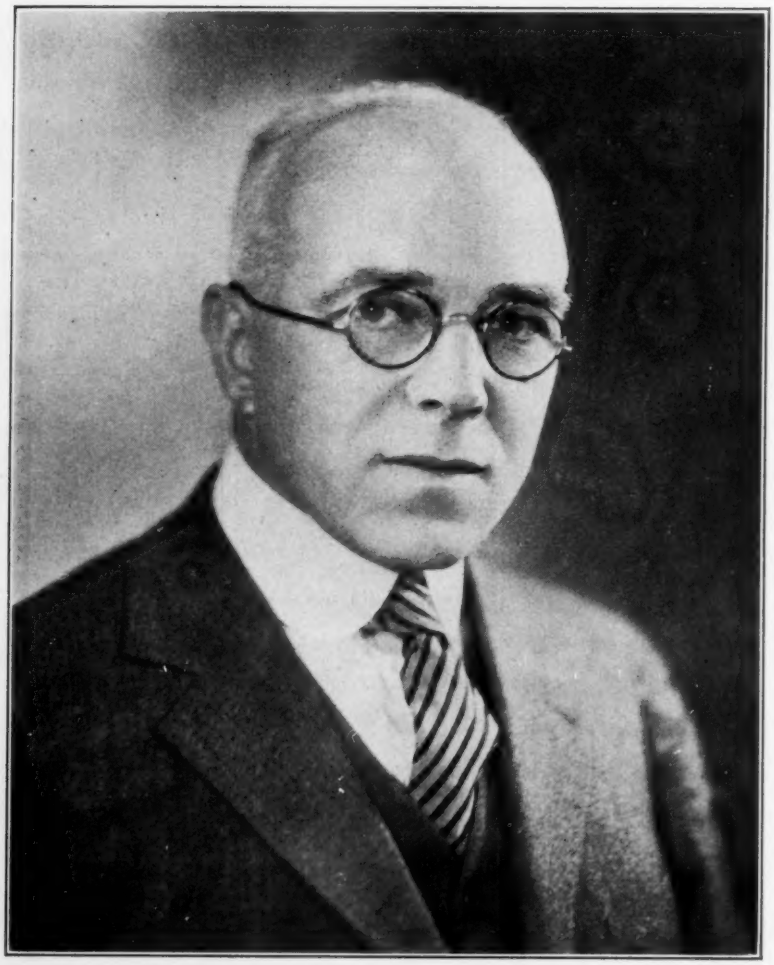
THE pharmacists of Maryland of every branch feel highly honored that the AMERICAN PHARMACEUTICAL ASSOCIATION will hold its seventy-eighth annual meeting over which a distinguished native son will preside, in Baltimore.

To me has been given the duty and privilege, as Local Secretary, of directing the arrangements for this meeting and for entertaining those who will attend it, we hope, in greater numbers than ever before. I have invited the presidents and secretaries of the eight pharmaceutical organizations of the state to act as an Executive Committee in conducting this meeting. Each of them has responded wholeheartedly and with every assurance that all will coöperate to insure the complete success of the meeting in every way.

SAMUEL Y. HARRIS.

We will not be able, on account of the fact that the meeting will be held so much earlier than is customary, to announce our plans in such detail as we should like to. Baltimore and Maryland have had close associations with the A. PH. A. since its organization and are proud of its history and accomplishments. We shall do our best to make our guests feel at home and enjoy their visit with us.

Hosts require guests in order to make hospitality possible and the more the merrier. My associates and I and all others in Maryland connected with pharmacy in any way cordially invite the members and friends of the A. PH. A. to meet with us, May 5–10, 1930. Governor Ritchie, Mayor Broening and other officials extended a similar invitation during the Rapid City meeting.



E. N. GATHERCOAL.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XIX FEBRUARY, 1930 No. 2

THE CHAIRMAN OF THE COMMITTEE ON NATIONAL FORMULARY.

Additional work and responsibilities were assigned to Chairman Gathercoal during 1929—he was elected to the chairmanship of the National Conference of Pharmaceutical Research, of the Committee on Unofficial Standards and, recently, of the Committee on National Formulary. Each one of these assignments requires ability, judgment, interest, strengthened by love for the work and the profession; the past records of the chairman speak for his success in the important undertakings, and his willingness to serve should and will, doubtless, enlist hearty cooperation under his direction.

Edmund Norris Gathercoal is a native of Illinois, where, in his teens, he engaged as drug store apprentice and, later, matriculated at the College of Pharmacy, from which institution he graduated in 1895. After further drug store experience, he entered business on his own account until, in 1907, he was elected instructor in Botany and Pharmacognosy by his *Alma Mater;* in 1924 he was advanced to professor of Pharmacognosy.

Professor Gathercoal published his first paper in 1909, and since then has added thirty or more contributions to pharmaceutical literature; in 1914, he was awarded the Ebert Prize for his research on "The Pharmacognosy of the Medicinal Rhamnus Barks." Recently he has reported valuable studies on color standards. He is Joint Editor of the 3rd edition, 1928, of "Kraemer's Pharmacognosy."

In 1905, the subject of this brief sketch became a member of the Illinois Pharmaceutical Association and of the AMERICAN PHARMACEUTICAL ASSOCIATION. He served as secretary of the Chicago Branch, A. PH. A. from 1913–1926, and as its president 1926–1928; he was chairman of the Scientific Section, A. PH. A., 1918–1919, and *First Vice-President* of the ASSOCIATION 1922–1923. He is and has been a member of other important committees than those heretofore named; among them, the U. S. P. Revision Committee.

Chairman Gathercoal is a regular attendant of the annual meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION, the minutes of which, and of the Sections, speak of his interest and activity in it.

EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase St., BALTIMORE, MD.

CLOSER RELATIONS OF THE MEMBERS OF THE MEDICAL AND KINDRED PROFESSIONS.

LIBERTY is taken in reprinting an appeal of *Modern Surgery* to its readers, because it is addressed to "Kindred Professions," and evidences a spirit of helpfulness and a desire to be of service; it follows:

"The physicians of this country should seek to bring together in closer relation pharmacists, physicians and dental surgeons. These professions should work together; it would be of great advantage to all. In an effort at amalgamation the medical societies should take the lead with the determination to consummate a closer interrelation, not only of the organized societies, but to promote more frequent social and professional contacts of the individuals of the kindred professions.

"The dental surgeon and the pharmacist are both specialists and their separation from the regular medical profession has effected no good for any of the professions and has been of no advantage to the public.

"The initiative in the establishment of closer relations should be taken by the parent group, the regular medical profession.

"Numerically physicians far exceed in number the dental surgeons or the pharmacists. Their medical organization is larger, but the physicians are not as effective through their organization as is the organization of either the dental surgeons or the pharmacists. This is truth, though it may shock many physicians who are so well acquainted with medical organization, and quite uninformed as to the effective organizations of both the dental surgeons and the pharmacists.

"In a later issue *Modern Surgery* hopes to discuss some of the interesting aspects of the pharmacal and dental organizations. Suffice here to say these smaller organizations have protected the members of their profession more successfully than has the organization of the larger profession protected its members.

"The standards of the ethical dental surgeon and of the ethical pharmacist are above reproach. Closer social contacts would mean much for the welfare and happiness of the members of the three professions and their families. An interrelation of the three societies would be of tremendous advantage to all three professions, more could be accomplished of public good. Doctor, investigate, then do your part."

There is much in the foregoing message that appeals to us and the substance of it has frequently been repeated in these columns; in fact the closing paragraphs of an editorial in the January JOURNAL, and another in this issue, written before reading the timely appeal of *Modern Surgery*, express related viewpoints. For a like purpose liberty is taken in presenting thoughts from the JOURNAL of January 1919, in these words—The application of right principles is essential to effect right relations; the attitude and spirit are all-important. The greatest service is rendered by the individual or the profession that coöperates to give the largest number the greatest opportunity for development, contributing the best service to humanity and thereby adding to the wealth and health of civilization. The following from the same source has related application:

The AMERICAN PHARMACEUTICAL ASSOCIATION should be so generally and well known that it gives the members a standing in the community as peers of their profession; the same applies relatively to other national and state associations. Mem-

bership in an association should mark the member as one who is associated with the best men in his profession, engaged in efforts to raise the standard of his calling and make it more deserving of public confidence. Association membership gives pharmacists a higher appreciation of their profession and also of those likewise engaged, and of those in related work—an inspiration to promote pharmacy and contend for its rightful recognition. We have both individual and collective responsibilities.

A PHARMACY CORPS IN THE U. S. ARMY.

THE Medical Department of the U. S. Army may not find it possible to follow the lines of the Pharmaceutical Corps in the French Army closely, but the French organization has proven its worth to such an extent that Senator P. Cazeneuve, from Rhône, in writing the preface for the book on the "Organization and Activities of the Pharmaceutical Service of the French Army" by Leon Varenne, Pharmacist Major of the Army, included a tribute "to their (pharmacists of the World War) devotion and patriotic service, although silently given, to which the historian must in justice render homage." He states further "this work of M. Varenne makes us love and respect the members of this select corps which have contributed in their modest sphere, most eminent service to the country." The French pharmaceutical military service during the World War rendered services that are inestimable, whether considered solely from the monetary value to their people, their military organizations, or as professional and humanitarian benefits. The French pharmaceutical corps has been publicly commended "as having proved to be one of the most effective, active and intelligent corps of the Frency Army."

The shortcomings of the French sanitary service in the Franco-German War led to a reorganization. The medical corps demanded exclusive direction and autonomy over the service, and that the pharmaceutical corps should become the subordinate and in consequence result in a systematic reduction of the military pharmacists. J. B. Dumas favored the placing of the sanitary service under the medical direction and administrative influence of pharmacy, and Medical Inspector General Legouest ardently advocated the preëminence of the medical over the pharmaceutical but declared that "the project must respect the cadre and rank of the military pharmacists and that there must be preserved to pharmacy all its rank, its appropriation, the condition of advancement and the various functions of its proper service."

In the late War the French profited by the aptitude of pharmacists and their professional education in preparing for attacks by irritating, asphyxiating and poisonous gases and, primarily, in the counteraction of the means used by the invaders; as a result the peacetime pharmaceutical service was largely extended.

There is a close relation of the German system and that of the French Army; recently, Sweden adopted that of the latter, and other countries of Europe, excepting Great Britain, have followed these lines of organization and activities quite closely.

A British medical writer, after the close of the War, spoke of the high position held by the pharmaceutical profession in the French Service. He said that "pharmacy had been described as the handmaiden of medicine; in the British Army

pharmacy is little more than a drudge, but in the French Army medicine and pharmacy enjoy equal rights and privileges."

It is unnecessary at this time to discuss the French pharmacy corps because such an organization in the U. S. Army would probably differ. Under the law of 1889 the French pharmaceutical cadre is composed of

1 Pharmacist Inspector, with rank of General of a brigade.
4 Pharmacist Principals, First Class, with rank of Colonel.
5 Pharmacist Principals, Second Class, with rank of Lieutenant-Colonel.
30 Pharmacist Majors, First Class, with rank of Chief of Battalion.
45 Pharmacist Majors, Second Class, with rank of Captain.
20 Pharmacist Aide-Majors, First Class, with rank of Lieutenant.
10 Pharmacist Aide-Majors, Second Class, with rank of Second Lieutenant.

During the War the list was increased.

The pharmaceutical corps in the French Army is recruited in part from students of pharmacy and in part fr[illegible] macy [illegible]duates who hold first-class diplomas.

The Japanese pharmacy corps organization is similar to that of Germany; the rank of Pharmacist General has been created and former Pharmacist Major General Watanabe has been advanced to this position.

It will not be questioned that the United States has pharmacists who are competent for the work required in military pharmacy. Loyalty to our country and the profession of pharmacy stimulates our desire to have full coöperation of pharmacists in public health matters and have the importance of pharmacy in the Government Services recognized; to this end it is hoped that those engaged in related professions will join in a spirit of altruism and unselfishness in the promotion of all divisions of medical service in behalf of those engaged in military activities as well as of those in civil life.

Charles Dawes' Creed—A Paraphrase.—"If you work in a profession, in Heaven's name work for it. If you live by a profession live for it. Help advance your co-worker. Respect the great power that protects you, that surrounds you with the advantages of organization, and that makes it possible for you to achieve results. Speak well for it. Stand for it. Stand for its professional supremacy. If you must obstruct or decry those who strive to help, why—quit the profession. But as long as you are a part of a profession do not belittle it. If you do you are loosening the tendrils that hold you to it and with the first high wind that comes along you will be uprooted and blown away and probably you will never know why."

"A PREMATURE PHARMACY CORPS DECISION?"

THE *Army & Navy Register* of January 18th states that "in the House on January 11th, Mr. Reece introduced a Bill (H. R. 8473) to provide for a pharmacist corps in the Army medical department. This is a measure which is urged by the Association of Pharmacists and has been before Congress in past sessions. It does not have the approval of the Surgeon General of the Army,

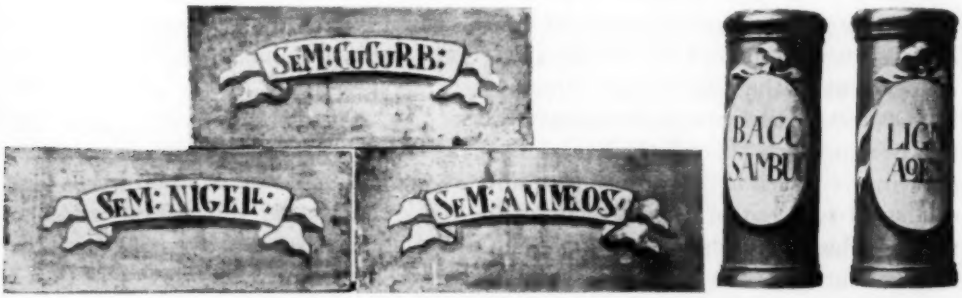
who has recommended against its adoption. *If it should pass the House and Senate and reach the President, it is destined to receive executive veto, on the representations that will be made by the Secretary of War.* The objections to the measure have been fully described in previous issues of this paper." (Italics ours.)

It is true that the *Army & Navy Register* did have an editorial in which the Pharmacy Corps Bill was mentioned but nothing has been said about the answer by Chairman R. L. Swain nor of the Hearing on the Bill."

We do not know how far the *Army & Navy Register* is authorized to speak for the Surgeon General, but we are not convinced that ***The President*** nor the ***Secretary of War*** authorized the *Register* to make for them such a statement as, seemingly, is indicated by the quoted editorial comment (see Italics). The statement—referring to "the Association of Pharmacists"—is indefinite and lacks completeness, the reference should have been plural or have mentioned the name of "the Association of Pharmacists"—there are eleven national associations of pharmacists and, excepting only one, each state has an association and in nearly all states there are local organizations, represen[illegible]-told, memberships of about 100,000 or more.

THE SWEDISH APOTHECARY SCHEELE HONORED ON SESQUICENTENNIAL OF HIS DISCOVERY OF GLYCEROL.

The debt of modern science and industry to Karl Wilhelm Scheele, the pharmacist and discoverer of glycerol, was recognized at the annual meeting in Chicago on December 11th of the Association of American Soap and Glycerin Producers. The association sent to Crown Prince Gustaf Adolf, honorary member of the Royal Academy of Sciences of Sweden, a message felici-



Drawers and containers for drugs from Scheele's pharmacy in Stockholm Museum—the latter are made of wood painted with cinnabar, the shields are white and rosettes of light blue color. The drawers are blue, the name in black on white background and the initial letters are red. The pharmacy (Apotheke) was established in 1759 in Köping and acquired by Scheele in 1776. The illustrations were reproduced from "D. A. V. Apotheker-Kalendar," 1930, Fritz Ferchl.

tating him on the part played by his country in the development of glycerol products. December 19th marked the one hundred and eighty-seventh anniversary of Scheele's birth, and 1930 marks the sesquicentennial of his discovery. Although regarded as relatively unimportant at the time, glycerol has come to be one of the most widely used substances known to science and industry.

First Aid Week—March 16th-22nd.

SCIENTIFIC SECTION

THE PHARMACOLOGY OF ERGOT.

(The bibliography will follow the last article of the series.)

PART V. PHARMACOLOGICAL STUDY OF FLUIDEXTRACT OF ERGOT, U. S. P. X.

BY MARVIN R. THOMPSON.[1]

The recent reports of other investigators referred to in the preceding articles of this series (37, 38, 39, 41) included extensive studies of the specific alkaloidal activity of crude ergot and its preparations. Owing to the general belief that the amines (histamine, tyramine, etc.) are not specific for the drug and are therefore of little importance, adequate studies of both groups of pharmaco-dynamically active constituents individually and in mixtures as they occur in the crude drug and in its galenicals, seem to be lacking.

Pattee and Nelson (28) and Swanson (34) found that the U. S. P. Cock's Comb Method (24) and the Broom-Clark Isolated Rabbit Uterus Method (13) yielded similar results in estimating the alkaloidal activity of ergot preparations. In marked contrast to the observations of these investigators, the writer found the two methods to yield widely discordant results in certain instances in extensive individual and collaborative assays of U. S. P. Fluidextracts of Ergot. Most of the collaborative studies involved the U. S. P. Cock's Comb Method only and, although the results obtained appeared very discouraging, a careful analysis of these results revealed certain rather striking information, as follows:

Of a total of 50 samples of the Fluidextracts of Ergot investigated, approximately 60 per cent yielded reasonably concordant results in the hands of the bio-assayists using the Cock's Comb Method. The results obtained from the remaining 40 per cent of the fluidextracts were at very great variance by the same method, lowest and highest results frequently differing by 200 to 300 per cent. Applying the Broom-Clark (13) Method to all of these samples, the author obtained results agreeing very well with the average results by the Cock's Comb Method in the case of the 60 per cent of fluidextracts. The remaining 40 per cent of the samples, which yielded discordant results by the Cock's Comb Method, gave results by the Broom-Clark Method appreciably higher than those obtained by the Cock's Comb Method.

A careful analysis of the types of fluidextracts involved in these studies revealed that the 60 per cent of samples yielding consistent and concordant results by both methods consisted of fluidextracts of various ages, some very recently prepared and others from four months to two years old. These samples in repeated assays by both methods at 2- or 3-month intervals continued to yield consistent results, showing a gradual decrease in potency as their ages increased.

The 40 per cent of fluidextracts yielding discordant results by the Cock's Comb Method, but consistently higher results by the Broom-Clark Method, consisted

[1] Assistant Pharmacologist, Food, Drug and Insecticide Administration, U. S. Department of Agriculture, Washington, D. C.

of fluidextracts which were invariably less than 6 months of age and for the most were freshly prepared at the time of distribution and less than 2 months old at the time of assay. Repeated assay of these fluidextracts by the Cock's Comb Method gave widely varying results even from day to day, making it almost impossible to determine the potency even approximately, as the birds did not respond consistently to varied doses, although the Broom-Clark Method continued to give consistent, though invariably higher, results. As the samples became older assays by the Cock's Comb Method showed an apparent increase in potency instead of an expected decrease. A gradual decrease in potency was shown by the Broom-Clark Method. After attaining an age of 6 to 8 months several of the fluidextracts had apparently doubled or more than doubled their original potency as shown by the Cock's Comb test. The highest value obtained upon the aged products by this method in several instances nearly reached the value shown by the first Broom-Clark Method assays. Strangely, after the samples had aged 6 or 8 months, the two methods gave similar values for a given fluidextract.

These observations indicate that: (1) Certain principles are contained in some Fluidextracts of Ergot of recent preparation in amounts sufficient to destructively interfere with the manifestation of alkaloidal potency by the Cock's Comb Method; (2) These interfering substances do not seriously influence results upon alkaloidal potency by the Broom-Clark Method; and (3) The interfering substances deteriorate to such an extent in 6 months (approximately) that they cease to exist in sufficient amounts to cause serious interference in estimating the alkaloidal potency by the Cock's Comb Method. These indications are substantiated by the experimental results which follow:

METHODS OF ASSAY.

The bio-assay methods used in this study of Fluidextracts of Ergot are the same as those described in Part IV of this series of reports (41) as follows:

(1) The Cock's Comb Method, official in U. S. P. X for the assay of Fluidextract of Ergot. The details of this method are described by Gittinger and Munch (15) and Pattee and Nelson (28).

(2) The Isolated Rabbit Uterus Method of Broom and Clark (13) for the Estimation of the Alkaloidal Activity of Ergot Preparations. The method as employed is described in detail by Pattee and Nelson (28).

(3) The Isolated Guinea-Pig Uterus Method for the estimation of the Non-specific Amine Activity of Fluidextract of Ergot. The details of this method were reported in Part II (38) of this series.

(4) The Pressor Method to Anesthetized Dogs. This method was described in Part IV of this series (41).

These studies were carried out primarily for the purpose of determining the cause of the discordant results obtained by the Cock's Comb Method in the case of freshly prepared fluidextracts previously discussed and, if possible, to develop some means of obviating the observed discrepancies by this method.

The Cock's Comb Method is generally reputed to measure the specific alkaloidal activity of ergot preparations (15, 28, 34, etc.). Yet it has been found that certain aqueous extracts high in non-specific amine activity may exhibit appreciable potency by this method, even when practically devoid of active ergot alkaloids (41), especially if the cockerels employed have previously undergone frequent ergot testing over an extended period.

The results in Tables I and II of Part IV of this series of articles and in Table III of this article definitely show that although the amines (histamine, tyramine, etc.) may exist in sufficient

amounts to cause bluing of the cock's comb if given in the absence of alkaloids, any cyanotic effect of the amines in fluidextracts does not add to that produced by the alkaloids.

The ten Fluidextracts of Ergot listed in Table III were freshly prepared according to the method of the U. S. P. from samples of crude ergot individually differing in alkaloid and amine content. They were tested from time to time, as indicated in Table III, by the Cock's Comb Method.

Changes in alkaloidal content were determined at the same intervals by the Broom-Clark Isolated Rabbit Uterus Method (28), and changes in the amine content by the Isolated Guinea-Pig Uterus Method (38).

TABLE III.—CHANGES OCCURRING IN FLUIDEXTRACTS OF ERGOT, U. S. P., AS OBSERVED BY BIO-ASSAY METHODS.

Fluidextracts, U. S. P. process. No.	Age of fluidextract at time of assay.	Potency by U. S. P. Cock's Comb Method (15). In Terms of U. S. P. Standard Fluidextract. *Per cent.*	Potency by Broom-Clark Method (28) for alkaloidal activity. In Terms of U. S. P. Standard Fluidextract. *Per cent.*	Total amines, calculated as histamine; by Isolated Guinea-Pig Uterus Method for amines of fluidextracts (38). *Per cent.*
20	1 day	130–150	140–150	0.012
	1 month	130–150	125–135	0.006
	3 months	120–135	120	0.004
	6 months	100–120	110	0.004
	9 months	100	100	0.004
21	1 day	200–250	225	0.010
	1 month	200–250	200–225	0.006
	3 months	175–200	200	0.006
	6 months	150–175	170–180	0.004
	9 months	150	150–160	0.004
22	1 day	130–200	250	0.045
	1 month	180–225	225	0.027
	3 months	180–200	200–210	0.012
	6 months	160–170	160–170	0.009
	9 months	100–120	120–130	0.005
23	1 day	50–100	110–120	0.065
	1 month	80–100	100	0.027
	3 months	60–80	70–80	0.015
	6 months	50–60	60–70	0.009
	9 months	40–60	50–60	0.007
24	1 day	100–350	425–450	0.150
	1 month	200–300	400–425	0.097
	3 months	250–330	375–400	0.042
	6 months	275–300	330–350	0.023
	9 months	250–275	280–300	0.012
25	1 day	400–450	440–450	0.027
	1 month	350–400	400–420	0.013
	3 months	300–350	330–350	0.009
	6 months	250–300	260–280	0.008
	9 months	200–250	230–250	0.005
26	1 day	150–300	370–400	0.087
	1 month	200–300	340–360	0.066
	3 months	250–300	300–325	0.027
	6 months	225–280	250–270	0.015
	9 months	200–250	200–225	0.010
27	1 day	130–150	150	0.008
	1 month	120–140	140–150	0.008
	3 months	120–140	130–140	0.005

	6 months	100–125	120–130	0.006
	9 months	80–100	100	0.006
28	1 day	75–350	400–420	0.125
	1 month	200–350	370–380	0.095
	3 months	200–330	330–350	0.066
	6 months	200–300	300–325	0.045
	9 months	200–250	250–270	0.037
29	1 day	100–200	200–220	0.075
	1 month	130–175	180–190	0.045
	3 months	140–175	160–170	0.033
	6 months	130–160	150	0.027
	9 months	120–140	130–140	0.015

TABLE IV.—COCK'S COMB ASSAY OF FLUIDEXTRACT NO. 24 IMMEDIATELY AFTER PREPARATION.

Bird no.	Threshold dose. *Cc./Kg.*	Intensity* of reaction from threshold dose.	Weight of bird. *Kg.*	Multiple of threshold dose.	Dose of F. E. No. 24 Injected. Per Kg. *Cc.*	Per bird. *Cc.*	Intensity of reaction* at end of 1 hr.	Intensity of reaction* at end of 1½ hrs.	Results: Percentage potency in terms of U. S. P. standard based on observation at end of 1 hr.	Results: Percentage potency in terms of U. S. P. standard based on observation at end of 1½ hrs.
554	0.5	122	1.630	1/5	0.100	0.163	012	001	<500	<500
1564	0.5	123	1.650	1/5	0.100	0.165	012	002	<500	<500
7193	0.7	123	1.580	1/4	0.175	0.276	112	122	<400	400
7210	0.5	123	1.610	1/4	0.125	0.201	122	123	400	400
2772	0.5	122	1.720	1/3	0.166	0.285	012	223	<300	>300
7471	0.6	123	1.650	1/3	0.200	0.330	123	223	300	>300
7124	0.4	023	1.510	2/5	0.160	0.242	123	233	250	>250
2721	0.6	123	1.550	2/5	0.240	0.372	123	223	250	>250
1790	0.5	022	1.690	1/2	0.250	0.423	233	233	>200	>200
7369	0.6	123	1.730	1/2	0.300	0.519	012	233	<200	>200
1482	0.7	123	1.660	3/4	0.525	0.872	102	233	<133	>133
7372	0.6	123	1.690	3/4	0.450	0.760	333	333	>133	>133
7466	0.5	023	1.500	1	0.500	0.750	013	133	<100	>100
6923	0.5	122	1.530	1	0.500	0.765	223	333	>100	>100
7302	0.5	123	1.570	1¼	0.625	0.981	233	333	> 80	> 80
6984	0.6	123	1.540	1¼	0.750	1.255	333	333	> 80	> 80
7545	0.7	123	1.760	1½	1.050	1.848	123	132	66	> 66
2836	0.5	122	1.690	1½	0.750	1.268	123	023	66	< 66
7382	0.6	123	1.490	2	1.200	1.788	123	223	50	> 50
7116	0.5	123	1.520	2	1.000	1.520	223	333	> 50	> 50

* The number code used to record the intensity of the cock's comb cyanosis is derived as follows:

1 indicates a barely perceptible reaction; *2*, a pronounced but sub-maximal effect; and *3*, a maximal reaction. The numerical expressions of intensity in Tables IV and V indicate readings from the anterior to the posterior portions of the comb. The anterior of the comb is usually affected less than the posterior. Thus "123" denotes the intensity usually produced by a "threshold" dose, *i. e.*, a satisfactory reaction, reading from anterior to posterior; "223" a proportionately greater reaction; and "333" a maximal discoloration from anterior to posterior, etc. An "023" reading, similarly, denotes no effect in the anterior third of the comb; a satisfactory cyanosis of the central portion, and a maximal reaction in the posterior third of the comb.

In standardizing cockerels, record is made of the effective dose, and also the intensity of reaction to that dose, since all combs do not react the same in all respects.

DISCUSSION OF RESULTS IN TABLE III.

The fluidextracts enumerated were very carefully and freshly prepared by the method of the U. S. P. and stored in amber-colored, tightly-sealed bottles in a cool room. The samples

were further protected from light by placing the bottles in a covered wooden box. Each fluidextract was physiologically assayed for amine and alkaloid potency immediately after preparation and at the various time intervals indicated in the table. Undue exposure of the fluidextracts to air was avoided by withdrawing the liquid with a hypodermic syringe, inserting the needle through the stopper. The crude drug samples entering into the preparation of the fluidextracts were purposely selected to show the influence of high and low proportions of amines upon the manifestation of alkaloidal potency by the Cock's Comb and Broom-Clark Isolated Rabbit Uterus Methods.

The potency values of the various fluidextracts by the Cock's Comb and Broom-Cark Methods are expressed in terms of the U. S. P. X Standard Fluidextract, the standard being taken as 100 per cent. In certain instances the results obtained by the Cock's Comb Method are indefinite. For instance, in the case of Fluidextract No. 24, when assayed immediately after preparation, different cockerels gave inconsistent results, varying from an apparent potency of 50 to 350 per cent of the U. S. P. standard, even though the birds had been carefully standardized in the usual manner (15, 28). At the same time, the Broom-Clark Method showed a potency of 440 to 450 per cent consistently in several assays.

To show the inconsistencies observed, the detailed cock's comb assay of freshly prepared Fluidextract No. 24 is given in Table IV.

The cock's comb results in Table IV for Fluidextract No. 24 of Table III are inconsistent, different cockerels showing a potency varying from 50 to 400 per cent U. S. P. Standard. The highest value shown by this cock's comb test agrees fairly well with that obtained by the Broom-Clark Method (Table III). The probability of error, however, is very great, as most of the birds show a potency appreciably less than 300 per cent, variations being so great as to actually prevent an estimation of the potency, even though 20 birds were used for the single sample. In attempting to reach an explanation for the inconsistent cock's comb results it was observed that the only apparent difference between this particular fluidextract and the fluidextracts yielding definite and consistent results by the same method lies in the unusually high amine activity. The results in Table III show that the non-specific amine concentration bears a direct relation to the magnitude of the inconsistencies met in the use of the Cock's Comb Method for estimating the specific alkaloidal activity of Fluidextract of Ergot. It is also shown that the amine activity deteriorates more rapidly than that of the alkaloids. As the amine activity deteriorated, the Cock's Comb Method yielded much more consistent results, most of the freshly prepared fluidextracts reaching a reasonably stabilized condition (as indicated by consistent cock's comb results) in approximately 4 months, even in samples originally having an extraordinarily high amine content.

In Article IV of this series (41) it was shown that the active non-specific amine fraction often exists in ergot in concentrations high enough to cause bluing of the cock's comb. The results in Tables III and IV show that any cyanosis produced by these amines does not add to that produced by the ergot alkaloids, for, if the effect were additive, results by the Cock's Comb Method would be higher than those obtained by the Broom-Clark Method which measures only the alkaloidal content. As the apparent potency shown by the Cock's Comb Method is never higher, but frequently lower than that shown by the Broom-Clark Method in the case of fluidextracts high in amine content, it is only logical to assume that the amines may exist in amounts sufficient to interfere destructively in the manifestation of alkaloidal potency as observed by the Cock's Comb Method. The success that has attended the use of the Cock's Comb Method in commercial application is undoubtedly due to the fact that many samples of crude ergot do not contain enough amines to cause interference in the assay of the resulting fluidextracts. Even those fluidextracts which do contain interfering quantities of amines when freshly prepared will lose the greater part of this amine activity before final assay and subsequent distribution if they are aged for six months as is specified in the U. S. P. for the Standard Fluidextract.

As is generally known, considerable lack of uniformity exists in commercial Fluidextracts of Ergot. This non-uniformity seems to be due largely to the interference of the non-specific amines in the estimation of specific alkaloidal activity by the official Cock's Comb Method. It is due also in part to the unstable nature of the specific alkaloids.

The individual pharmaco-dynamically active constituents of ergot are available in the pure state. If the conclusions based upon the foregoing observations on the destructive amine interference in assaying certain freshly prepared fluidextracts by the Cock's Comb Method are

correct, it should be possible to show this interference by studying the effects of these individual constituents singly and in mixtures using the Cock's Comb Method. This study, therefore, was undertaken.

MANIFESTATIONS OF ACTIVITY OF THE INDIVIDUAL ACTIVE CONSTITUENTS OF ERGOT AS SHOWN BY THE COCK'S COMB METHOD.

1. The Specific Ergot Alkaloids.

Two alkaloids, ergotamine and ergotoxine, are responsible for practically the entire alkaloidal activity of ergot. These two alkaloids exhibit identical pharmaco-dynamic reactions. Therefore, either one may be regarded as entirely representative of the alkaloidal activity of ergot. Both have been extensively used in these studies. As the results in all instances were identical, however, only those obtained from ergotamine will be discussed.

The ergotamine solution was prepared by dissolving crystalline ergotamine tartrate in water in a concentration such that 1.0 cc. of the solution represented 0.5 mg. of ergotamine base. (Ergotamine tartrate used corresponds to approximately 84.5% ergotamine base.) A bare trace of hydrochloric acid was added to facilitate solution. This particular concentration was selected because it closely approximates that of U. S. P. Fluidextract of Ergot with respect to alkaloidal activity.

Injections were made deep into the pectoral or breast muscles in the usual manner. Other details of technique as described in the U. S. P. were observed.

In experiments involving over 250 injections to 50 carefully standardized white Leghorn cockerels of U. S. P. specifications, the following results were obtained:

(*a*) Ergotamine, in suitable doses, consistently produced the characteristic bluing or cyanosis of the cock's comb in all instances.

(*b*) As in the case of Fluidextract of Ergot, the intensity of the cock's comb reaction produced by ergotamine was directly proportional to dosage within maximum and minimum limits.

(*c*) Different cockerels varied with respect to the intensity of reaction produced by a given dose of ergotamine. Once the threshold dose (15, 28) had been established, however, the individual cockerels responded consistently to that dose for two to four months, if a 2-week rest period between injections (24) was given. Although cockerels varied in susceptibility to ergotamine, most of those used in these studies exhibited a barely perceptible cyanosis from the intramuscular injection of 0.10 to 0.20 mg. of ergotamine base per kilogram body weight. A pronounced but sub-maximal bluing was produced by 0.15 to 0.30 mg., and a maximal effect was usually observed when doses of 0.30 mg. or more per kilogram body weight were injected, observations being recorded approximately one hour from the time of injection.

(*d*) Ergotamine, in doses just sufficient to produce a perceptible cyanosis of the comb in one hour, gave no other characteristic significant symptoms in the cockerels. Respiration and pulse were not affected to any degree discernible by simple observation.

The bluing of the combs became evident in approximately 30 minutes in most instances, registering greatest effect in approximately one hour. The posterior lobe of the combs showed greater discoloration than the anterior. After persisting at this intensity for an additional one-half to 1 hour, the bluing gradually lessened. Some birds returned to apparent normality in five or six hours, although in most instances a longer period was necessary, occasionally as much as four or five days. Slightly greater doses, producing a pronounced but sub-maximal cyanosis of the comb, however, in some instances caused a slight manifestation of general symptoms. The characteristic bluing of the comb began to appear in the posterior lobe in approximately 30 minutes, increasing in intensity and gradually spreading toward the anterior, showing greatest

effect in 45 to 90 minutes, the time varying with different birds. At this point respiration was mildly stimulated in a few instances, but no symptoms other than the cyanosis of the comb were significantly in evidence. The discoloration usually persisted at this intensity for two hours or more before gradually receding. Return of the combs to normal required from four to ten days, the time for complete recovery varying greatly for individual birds. The posterior lobes of the comb always showed a more intense bluing than the anterior portions. The anterior portions usually cleared in 1 to 2 days, while the posterior lobes cleared much more slowly, occasionally requiring 15 to 20 days for recovery but usually attaining normality in less than two weeks. Still greater doses, just sufficient to produce a maximal bluing of the comb (0.3 to 0.5 mg. per Kg.), frequently caused the appearance of a preliminary respiratory and cardiac stimulation in 15 or 20 minutes, which gradually gave way to symptoms of slight depression, although no evidence of tremors, muscular incoördination or weakness resulted. The characteristic cyanosis of the comb appeared in the posterior lobes in 15 to 20 minutes, gradually increasing in intensity and spreading toward the anterior portions until a maximal reaction was observed in 45 to 90 minutes. This intensity usually persisted for two to six hours, after which the normal color began to return in the anterior portions of the combs. Several days were usually required for complete recovery of the combs, although in many instances more than 10 days were necessary.

(*e*) By using carefully standardized white Leghorn cockerels, *i. e.*, those whose threshold dose had been accurately determined, it was found possible to detect variations in dosage of as little as 0.05 mg. per Kg. of Ergotamine by the U. S. P. Cock's Comb Method. Accepting the values of Nelson and Pattee (28) and Swanson (34) of approximately 0.5 mg. of ergot alkaloids per cc. in terms of ergotamine or ergotoxine for U. S. P. Fluidextract of Ergot, a variation of ±0.05 mg. ergot alkaloids per cc. corresponds to a variation of ±0.1 cc. of fluidextract. Evaluating the U. S. P. Fluidextract as 100%, with the U. S. P. dose requirement of 0.5 cc. per Kg. to cockerels, a ±0.1-cc. variation corresponds to ±20% U. S. P. X Potency.

Thus, with a simple solution of pure ergot alkaloids, the U. S. P. X Cock's Comb Method could be depended upon to yield estimates of alkaloidal potency within ±20% of the potency of the U. S. P. Fluidextract in all assays, and in many instances even a greater accuracy was observed, frequently with only a ±10% U. S. P. potency variation.

(*f*) Continued usage of the cockerels every two weeks for 6 to 8 months, the time covered by the experiments here described, caused no apparent change in their response to ergot alkaloids, with the exception of slight changes in threshold reactions, necessitating restandardization of the birds every two or three months. The cockerels invariably were found to increase in susceptibility from continued use.

2. *Histamine.*

Histamine is generally conceded to be the most important of the amines associated with ergot from the standpoint of pharmaco-dynamic activity and occurrence in the drug. This has been confirmed by the experimental results of this investigation.

With this information at hand, and the fact that certain aqueous extracts of ergot high in amine content but practically devoid of alkaloids frequently exhibited appreciable potency by the Cock's Comb Method (see Part IV) (41), there arose the possibility that histamine probably sometimes existed in amounts sufficient to cause bluing of the cock's comb. In spite of the fact that the Cock's Comb Method is reputed to measure only the alkaloidal activity of ergot preparations, histamine alone often produced upon the comb of cockerels an effect closely resembling that produced by ergot alkaloids.

From the very beginning of these experiments it was noted that, although the general symptoms produced by intramuscular injections of histamine to various cockerels were fairly consistent, the bluing or cyanosis of the comb was produced much more easily and to a greater degree of intensity on birds that had been used for ergot testing every two weeks for from 6 months to 1 year than on new birds

which had received but a few injections of ergot preparations. The results obtained from both types of cockerels will therefore receive consideration.

(*a*) *Old Cockerels of U. S. P. Specifications Regarding Type and Weight.*—These birds had been used every two weeks for 6 to 12 months for testing ergot preparations. Results reported include only those obtained from 20 birds having a threshold (15, 28) of 0.5 cc. U. S. P. Standard Fluidextract of Ergot per kilogram body weight, to obviate the necessity of tabulating all results from birds showing different susceptibility or tolerance.

As in the consideration of ergot alkaloids, three ranges of doses of histamine, determined by the intensity of the comb cyanosis, have been studied.

Intramuscular doses of less than 0.5 mg. per Kg. were invariably ineffective in producing any change in the appearance of the combs. Slight symptoms of general depression became evident in a minority of instances. Doses of 0.75 mg. of histamine per Kg. reacted as follows:

The first perceptible effect usually became evident in 20 to 30 minutes. The combs began to blanch, respiration and pulse became a bit more rapid. As time elapsed the blanching of the combs increased and began to show bluing. Respiration and pulse became slower, with symptoms of general depression, muscular weakness and incoördination. Greatest effect was usually observed approximately 40 minutes from the time of injection. No symptoms were significantly in evidence except for the general depression and the blanching or bluing of the combs. Two hours from the time of injection invariably found all cockerels restored to apparent normality, with the combs clear and red.

Cockerels receiving 1.0 mg. histamine per Kg. reacted in a similar manner except that all symptoms developed slightly sooner and attained a greater intensity. The bluing and blanching of the combs became clearly evident; the preliminary brief stimulation of pulse and respiration quickly gave way to marked general depression and muscular weakness, coupled with incoördination and tremors. These effects usually had reached their greatest intensity in 1 to $1^1/_2$ hours after injection, after which they began to recede. In 3 or 4 hours all cockerels had apparently returned to normal, with their combs a bright red.

Doses of 1.5 mg. of histamine reacted in a comparable manner, although to a proportionately greater intensity, showing a maximal effect in approximately 45 minutes. The combs became intensely blanched and blued, and a very marked general depression was manifest, with prostration in several instances and severe muscular weakness, incoördination and tremors in all instances. Recovery usually began within two hours and all birds had apparently returned to normal with a clear comb within an over night period.

Thus, it was observed that histamine was capable of producing a cyanosis of the cock's comb which was comparable to that produced by the specific ergot alkaloids, although other symptoms were vastly different. Since it has been shown (41) that histamine frequently exists in crude ergot to the extent of 1.0 mg. per gram of drug, and that the total amount of histamine and other amines is completely extracted by the menstrua employed in the manufacture of ergot preparations, it is evident that an appreciable potency may be observed by the Cock's Comb Method, even though no alkaloids are present. The amine potency, however, could not equal that of the U. S. P. Fluidextract in any of the samples examined because it would require 1.0 cc. per Kg., *i. e.*, twice the volume specified in the official method, to produce the desired reaction, indicating only 50% of the U. S. P. X potency for fluidextracts. A cock's comb potency of 100% U. S. P. X for any fluidextract would therefore indicate the presence of an appreciable quantity of ergot alkaloids.

(*b*) *New Cockerels.*—This group of birds comprised birds of the same type as those in (*a*), but they had never undergone ergot testing except for the several injections of Standard Fluidextract necessary to establish their threshold doses.

Although it is usually accepted that continued usage of cockerels for ergot testing does not alter their response to the active constituents of the drug, aside from slight changes in susceptibility, these studies have shown that the combs of new cockerels are not affected by histamine nearly as easily as those of birds used over an appreciable period of time, even though the response of both types was identical for the alkaloids or the Standard Fluidextract. The symptoms of depression and muscular weakness could be produced by the usual doses, but the combs

occasionally showed no appreciable effect, even in doses of 1.5 mg. per Kg. In most instances, however, at least a slight blanching or bluing of the comb was produced.

3. *Mixtures of Ergot Alkaloids and Histamine.*

The assay results obtained from fluidextracts high in amine content (Tables I, III and IV) indicated that the active amines interfered with the manifestation of alkaloidal potency by the Cock's Comb Method, *i. e.*, the amine fraction was

TABLE V.—RESPONSE OF SIX COCKERELS* TO ERGOTAMINE AT 2-WEEK INTERVALS FOR 10 WEEKS AND THE DESTRUCTIVE INTERFERENCE OF HISTAMINE ADMIXTURE UPON THE MANIFESTATION OF ALKALOIDAL ACTIVITY.

Cockerel no.	Ergot constituent injected Feb. 26, 1929.	Dose per Kg. *Mg.*	Intensity of comb reaction at end of one hour.	Ergot constituent injected Mar. 12, 1929.	Dose per Kg. *Mg.*	Intensity of reaction at end of one hr.
1	Ergotamine	0.20	123	Ergotamine	0.20	123
2	Ergotamine	0.20	112	Ergotamine	0.20	112
3	Ergotamine	0.225	123	Ergotamine	0.225	123
4	Ergotamine	0.25	223	Ergotamine	0.25	223
5	Ergotamine	0.30	223	Ergotamine	0.30	233
6	Ergotamine	0.40	333	Ergotamine	0.40	333
	March 26, 1929.			April 9, 1929.		
1	Ergotamine	0.20		Ergotamine	0.20	
	plus		123	plus		012
	Histamine	0.20		Histamine	0.20	
2	Ergotamine	0.20		Ergotamine	0.20	
	plus		012	plus		123
	Histamine	0.30		Histamine	0.30	
3	Ergotamine	0.225		Ergotamine	0.225	
	plus		002	plus		012
	Histamine	0.40		Histamine	0.40	
4	Ergotamine	0.25		Ergotamine	0.25	
	plus		022	plus		122
	Histamine	0.50		Histamine	0.50	
5	Ergotamine plus	0.30		Ergotamine plus	0.30	
	Histamine plus	0.60	123	Histamine plus	0.60	012
	Tyramine	0.20		Tyramine	0.20	
6	Ergotamine plus	0.40		Ergotamine plus	0.40	
	Histamine plus	0.75	122	Histamine plus	0.75	012
	Tyramine	0.20		Tyramine	0.20	
	April 23, 1929.			May 7, 1929.		
1	Ergotamine	0.20	123	Ergotamine	0.20	122
2	Ergotamine	0.20	122	Ergotamine	0.20	123
3	Ergotamine	0.225	123	Ergotamine	0.225	223
4	Ergotamine	0.25	223	Ergotamine	0.25	223
5	Ergotamine	0.30	233	Ergotamine	0.30	223
6	Ergotamine	0.40	333	Ergotamine	0.40	333

* These cockerels had been used every two weeks for four months or more in testing ergot preparations. The tests were made on the following dates: February 26, 1929; March 12, 1929; March 26, 1929; April 9, 1929; April 23, 1929; May 7, 1929.

antagonistic to the alkaloidal fraction as indicated by the comb cyanosis or discoloration, or, that the apparent potency is often lower than the actual alkaloidal potency.

In experiments involving the injection of mixtures of ergot alkaloids or amine-free fluidextracts, with histamine or alkaloid-free Aqueous Extracts in various proportions, this amine-interference has been repeatedly demonstrated.

Table V shows the consistent response of six cockerels to ergotamine at 2-week intervals and the effect of histamine in diminishing the response of the combs to ergotamine. Final repetitions of the ergotamine doses at 2-week intervals are recorded to show that changes in the reactions of the birds were not so variable as to cause the discrepancies noted in the injection of mixtures of amines and alkaloids.

The proportion of histamine to ergotamine that will produce a partial neutralization of effect on the cock's comb has been found exceedingly variable. In several instances, birds were injected with doses of ergotamine and histamine in proportions such that no effect was apparent at the end of an hour. Use of these same proportions in other experiments failed to show such marked antagonism between the two substances, although the manifestation of alkaloidal activity was usually diminished to some extent. In no instance was histamine capable of adding to the cyanosis produced by the alkaloids.

These observations have been duplicated by the addition of alkaloid-free aqueous extracts high in amine content to fluidextracts rich in alkaloidal activity but which were practically amine-free. While the amine content of ergot is exceedingly variable, it was found sufficiently high in a number of instances to cause marked interference in estimating the alkaloidal activity of ergot preparations by the U. S. P. X Cock's Comb Method, especially if the cockerels employed had been subjected to ergot testing for an appreciable period. It is believed that this factor of error explains the discrepancies observed in the cock's comb results recorded in this and preceding articles of this series, since it was observed that histamine caused interference even though the concentration present was not high enough to cause bluing of the combs in the absence of ergot alkaloids.

If a sufficient number of carefully standardized cockerels are employed, and all other details of the official method are properly observed, a correct interpretation of the results obtained reveals much information as to the nature and activity of Fluidextract of Ergot, as follows:

If results are not consistently accurate to within $\pm 20\%$ it is highly probable that appreciable quantities of amines are present. Symptoms other than the comb effect also must be observed. If the combs of different birds respond consistently to graded dosage, it is highly probable that the activity of the fluidextract is due entirely to the alkaloids present. Should a preparation produce comb cyanosis only from doses much greater than the predetermined "threshold dose," and the comb reaction is associated with symptoms of marked depression (described under Histamine), it is probable that the effect is due largely to the histamine present. Such a condition is never encountered with the U. S. P. Fluidextract, but occasionally is manifest by aqueous or semi-solid extracts of ergot.

It is a fact that any fluidextract prepared by the U. S. P. method contains appreciable quantities of ergot alkaloids if a satisfactory reaction is obtained from threshold doses of the preparation, regardless of the amine content. Any interference caused by the possible presence of appreciable quantities of amines will result in a low apparent alkaloidal potency as shown by the official method. *In other words, a sample of crude ergot meeting the U. S. P. biological requirements always contains at least as much alkaloidal activity as is indicated by the cock's comb test, and, if interfering quantities of amines also are present, the actual alkaloidal content will be greater than the amount indicated by the test.*

THE BROOM-CLARK ISOLATED RABBIT UTERUS METHOD.

A study of the Broom-Clark Isolated Rabbit Uterus Method, together with the details of its technique, was first reported by the originators (13). Further studies have been reported by Nelson and Pattee (1) Pattee and Nelson (28), Swanson (34), Rothlin (31) and others. A detailed description of the technique

occasionally showed no appreciable effect, even in doses of 1.5 mg. per Kg. In most instances, however, at least a slight blanching or bluing of the comb was produced.

3. *Mixtures of Ergot Alkaloids and Histamine.*

The assay results obtained from fluidextracts high in amine content (Tables I, III and IV) indicated that the active amines interfered with the manifestation of alkaloidal potency by the Cock's Comb Method, *i. e.*, the amine fraction was

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	March 26, 1929.			April 9, 1929.		
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	Histamine	0.20		Histamine	0.20	
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	plus		012	plus		123
	Histamine	0.30		Histamine	0.30	
3	Ergotamine	0.225		Ergotamine	0.225	
	plus		002	plus		012
	Histamine	0.40		Histamine	0.40	
4	Ergotamine	0.25		Ergotamine	0.25	
	plus		022	plus		122
	Histamine	0.50		Histamine	0.50	
5	Ergotamine	0.30		Ergotamine	0.30	
	plus			plus		
	Histamine	0.60	123	Histamine	0.60	012
	plus			plus		
	Tyramine	0.20		Tyramine	0.20	
6	Ergotamine	0.40		Ergotamine	0.40	
	plus			plus		
	Histamine	0.75	122	Histamine	0.75	012
	plus			plus		
	Tyramine	0.20		Tyramine	0.20	
	April 23, 1929.			May 7, 1929.		
1	Ergotamine	0.20	123	Ergotamine	0.20	122
2	Ergotamine	0.20	122	Ergotamine	0.20	123
3	Ergotamine	0.225	123	Ergotamine	0.225	223
4	Ergotamine	0.25	223	Ergotamine	0.25	223
5	Ergotamine	0.30	233	Ergotamine	0.30	223
6	Ergotamine	0.40	333	Ergotamine	0.40	333

* These cockerels had been used every two weeks for four months or more in testing ergot preparations. The tests were made on the following dates: February 26, 1929; March 12, 1929; March 26, 1929; April 9, 1929; April 23, 1929; May 7, 1929.

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Table V shows the consistent response of six cockerels to ergotamine at 2-week intervals and the effect of histamine in diminishing the response of the combs to ergotamine. Final repetitions of the ergotamine doses at 2-week intervals are recorded to show that changes in the reactions of the birds were not so variable as to cause the discrepancies noted in the injection of mixtures of amines and alkaloids.

The proportion of histamine to ergotamine that will produce a partial neutralization of effect on the cock's comb has been found exceedingly variable. In several instances, birds were injected with doses of ergotamine and histamine in proportions such that no effect was apparent at the end of an hour. Use of these same proportions in other experiments failed to show such marked antagonism between the two substances, although the manifestation of alkaloidal activity was usually diminished to some extent. In no instance was histamine capable of adding to the cyanosis produced by the alkaloids.

These observations have been duplicated by the addition of alkaloid-free aqueous extracts high in amine content to fluidextracts rich in alkaloidal activity but which were practically amine-free. While the amine content of ergot is exceedingly variable, it was found sufficiently high in a number of instances to cause marked interference in estimating the alkaloidal activity of ergot preparations by the U. S. P. X Cock's Comb Method, especially if the cockerels employed had been subjected to ergot testing for an appreciable period. It is believed that this factor of error explains the discrepancies observed in the cock's comb results recorded in this and preceding articles of this series, since it was observed that histamine caused interference even though the concentration present was not high enough to cause bluing of the combs in the absence of ergot alkaloids.

If a sufficient number of carefully standardized cockerels are employed, and all other details of the official method are properly observed, a correct interpretation of the results obtained reveals much information as to the nature and activity of Fluidextract of Ergot, as follows:

If results are not consistently accurate to within $\pm 20\%$ it is highly probable that appreciable quantities of amines are present. Symptoms other than the comb effect also must be observed. If the combs of different birds respond consistently to graded dosage, it is highly probable that the activity of the fluidextract is due entirely to the alkaloids present. Should a preparation produce comb cyanosis only from doses much greater than the predetermined "threshold dose," and the comb reaction is associated with symptoms of marked depression (described under Histamine), it is probable that the effect is due largely to the histamine present. Such a condition is never encountered with the U. S. P. Fluidextract, but occasionally is manifest by aqueous or semi-solid extracts of ergot.

It is a fact that any fluidextract prepared by the U. S. P. method contains appreciable quantities of ergot alkaloids if a satisfactory reaction is obtained from threshold doses of the preparation, regardless of the amine content. Any interference caused by the possible presence of appreciable quantities of amines will result in a low apparent alkaloidal potency as shown by the official method. *In other words, a sample of crude ergot meeting the U. S. P. biological requirements always contains at least as much alkaloidal activity as is indicated by the cock's comb test, and, if interfering quantities of amines also are present, the actual alkaloidal content will be greater than the amount indicated by the test*

THE BROOM-CLARK ISOLATED RABBIT UTERUS METHOD.

A study of the Broom-Clark Isolated Rabbit Uterus Method, together with the details of its technique, was first reported by the originators (13). Further studies have been reported by Nelson and Pattee (1) Pattee and Nelson (28), Swanson (34), Rothlin (31) and others. A detailed description of the technique

involved need not be repeated here. Briefly, the method depends upon the ability of the active alkaloids of ergot to inhibit the response of suitable strips of isolated rabbit uterus to constant epinephrine concentrations. As the amines associated with ergot are not capable of causing this inhibition of the epinephrine response, the method serves to estimate the alkaloidal activity of ergot preparations. Pattee and Nelson (28), however, found that the amines may cause interference by accentuating the epinephrine response, even though they are not present in sufficient amounts to cause contraction of the tissue by themselves. This, of course, would cause the results to indicate a slightly lower alkaloidal potency than was actually present because a greater concentration of ergot alkaloids would be

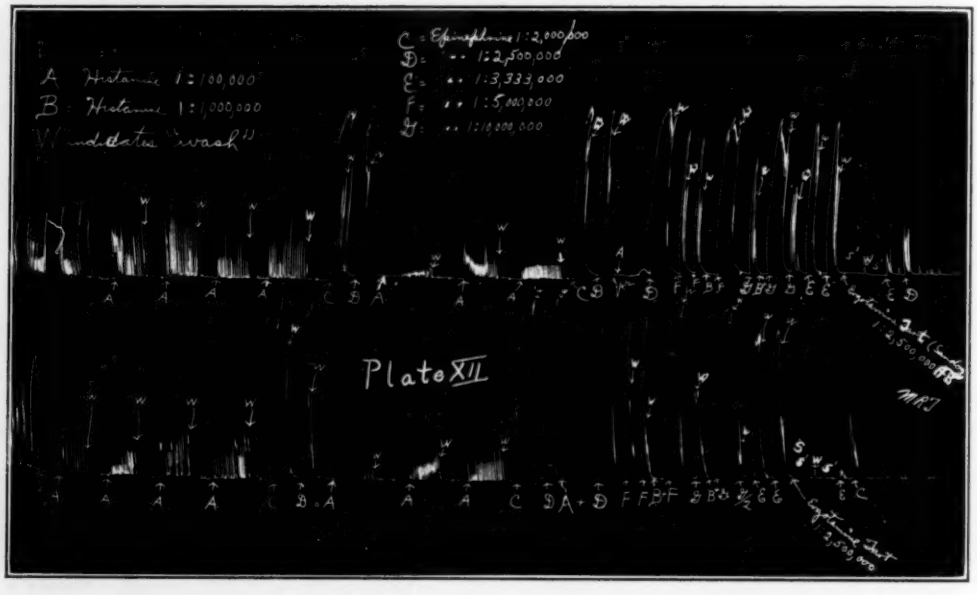


Plate XII.—The response of two similar strips of isolated Rabbit Uterus to histamine; epinephrine; epinephrine in the presence of stimulant and non-stimulant concentrations of histamine; and the similar inhibition produced by ergotamine alone (lower tracing), and in mixture with histamine (upper tracing) observed when both strips are washed at the end of five minutes. Note the inhibiting influence of epinephrine upon the response to histamine, and the effect of histamine admixture in accentuating the epinephrine response.

required to produce a given inhibition of the amine-accentuated epinephrine response of the uterine strips than would be required were the amines not present. Pattee and Nelson observed that the amine interference could be obviated by washing after permitting the alkaloids to act for five minutes, refilling the chambers with the saline solution and observing the final epinephrine response at the end of another five minutes.

The results obtained in the author's investigation tend to confirm these observations and are typified by the record in Plate XII. A careful study of this tracing shows, on two similar strips of isolated rabbit uterus: (*a*) the rhythmic contractions produced by stimulating concentrations of histamine; (*b*) the tonic contractions produced by epinephrine; (*c*) a loss of response to histamine after the administration of epinephrine; (*d*) the gradual return of response

to histamine; (*e*) the ability of histamine in stimulant and non-stimulant concentrations to accentuate the epinephrine response; (*f*) the constant response of both strips to epinephrine in similar concentrations; (*g*) the similarity of the inhibition produced by ergotamine in the presence of histamine (upper tracing) and the inhibition produced by the same concentration of ergotamine in the absence of histamine (lower tracing) obtained by observing the washing technique described by Pattee and Nelson (28).

This method has been used in estimating the alkaloidal content of all types of ergot preparations in these studies and, by employing a washing technique similar to that used and described by Pattee and Nelson (28), consistent results were obtained, irrespective of the amine content. The details of the method were described by the above authors. Without repeating the details of the method the writer has found that greatest accuracy may be obtained by observing the following precedure:

(*1*) Subject both of the similar strips to various concentrations of epinephrine until a concentration is found which will produce, upon several repetitions, constant and appreciable but sub-maximal contractions.

(*2*) Adjust the weights on the levers so that contractions of equal magnitude are obtained from each strip. This, of course, necessitates the use of levers of equal length, with the fulcrums at equal distances from the points of the strip attachments.

(*3*) After obtaining identical and constant sub-maximal response of both strips to a determined epinephrine concentration, and after all other factors (oxygen supply, temperature, etc.) are identical for each strip, permit the set-up to stand unmolested for exactly five minutes. Then drain and refill both strip chambers and allow them to stand exactly five minutes more. At this point again determine the epinephrine response. If the response of both strips is still identical, all is in readiness for the addition of the properly diluted ergot preparations. Place the standard preparation (either a solution of one of the alkaloids or the U. S. P. Standard Fluidextract) in one chamber and the unknown preparation in the other, carefully noting the time in each case. Allow the ergot preparations to act exactly five minutes on each strip, then wash, and let stand for exactly five minutes more. Then repeat the predetermined dose of epinephrine and observe the response. If a contraction is produced in both strips, repeat the epinephrine dose as a check. The second response is usually less than the first because the time which has elapsed permits the furtherance of the ergot alkaloid effect. Failure of the strips to contract shows that the ergot concentration administered was too great and the epinephrine response has been completely abolished. In such a case, add a larger dose of epinephrine, not that the response thus obtained is accurately significant, but it often serves to indicate roughly how much to decrease the concentration of the ergot preparation in the next experiment.

(*4*) Only one trial on a single pair of strips is possible because of the persistence of the effect of the ergot alkaloids, regardless of the amount of washing to which the strips are subjected. Therefore, fresh uterine strips are required for each determination.

(*5*) The concentration of ergot employed should be sufficient to produce not more than a 75 per cent inhibition nor less than a 50 per cent inhibition.

(*6*) An assay is complete only when a quantity of an unknown preparation which will produce the same inhibition as a definite amount of the standard preparation is determined.

This method is somewhat tedious and difficult of technique. After a reasonable amount of experience is attained, however, it has been found exceedingly accurate in estimating the specific alkaloidal activity of ergot preparations, provided a sufficient number of trials are made upon a single sample. Pattee and Nelson (28) and Swanson (34) found the method to be accurate within $\pm 10\%$, which is considerably more accurate than the present official method. The writer has found the method accurate to this degree in all instances. A $\pm 10\%$ variation in potency corresponds to a variation of approximately $\pm 0.005\%$ of ergot alkaloids, based on the strength of U. S. P. Fluidextract found by Pattee and Nelson (28). Plus or minus 0.005% ergot alkaloids corresponds to 0.05 mg. per cc. A variation of this size in the concentration of ergot alkaloids in an ergot preparation is easily detectable by the Isolated Rabbit Uterus Method.

PRESSOR METHODS TO ANESTHETIZED DOGS.

The Pressor Methods to anesthetized dogs are so well known that they need not be described here. A review of the literature reveals many attempts to apply

Plate XIII.—The effect produced by the intravenous administration of 0.2 cc. of the freshly prepared Fluidextract (by the U. S. P. Method to dog). Note the initial fall in blood pressure followed by a slight rise and another fall, indicating that a very appreciable quantity of Histamine has found its way into this preparation and that it has almost totally prevented a manifestation of alkaloidal response. By aging this preparation, the Histamine effect steadily diminished until finally the effect produced was entirely analogous to that of the pure specific alkaloid Ergotamine. Time in seconds.

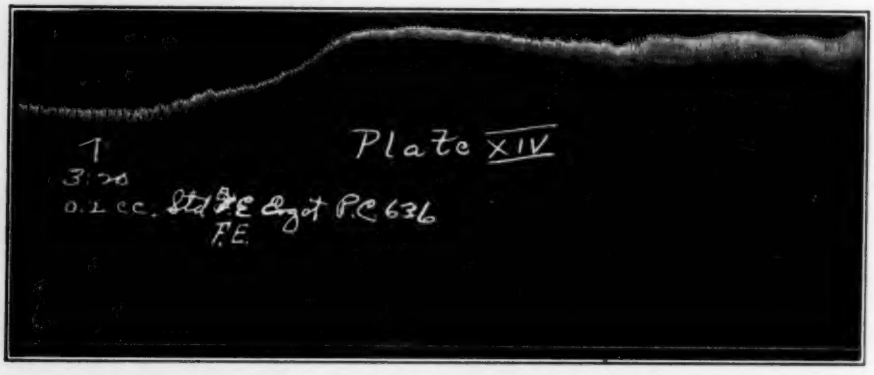


Plate XIV.—The effect produced upon the blood pressure of a dog by the intravenous administration of 0.2 cc. of Standard Fluidextract of Ergot. Note the absence of Histamine effect and the similarity between this rise in blood pressure and that shown in Plate VIII of Part IV (41).

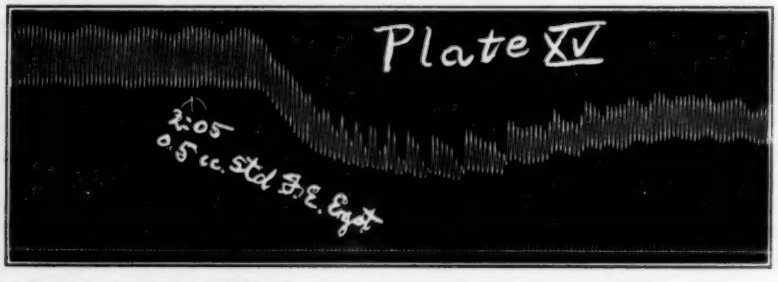


Plate XV.—Showing a reversal of the normal rise in blood pressure resulting when a dose of 0.5 cc. of the Standard Fluidextract of Ergot is preceded by a dose of Histamine or Aqueous Extract of Ergot. Histamine is capable of reversing the effect of the ergot alkaloids.

these methods in assaying ergot preparations. While the pressor reactions produced by the intravenous administration of the various constituents of ergot

are characteristic, the appearance of these constituents in mixtures, such as usually exists in fluidextracts, practically precludes their application quantitatively for the following reasons:

(*a*) The water-soluble amine fraction of the active constituents of ergot often exists in ergot preparations (especially fluidextracts) in amounts sufficient to cause a fall in blood pressure which may mask the pressure-raising effect of the specific alkaloids (Plate XIII), a condition comparable to that observed when a mixture of histamine and ergotamine is administered (Plate XI of Article IV (41)).

(*b*) The active ergot alkaloids produce a rise in blood pressure (Plate VIII, Article IV (41)). Repeated administration of identical doses of ergot alkaloids results in diminishing response, even when the doses are given at intervals of an hour.

(*c*) Injection of a preparation containing histamine results in a fall in blood pressure. If, after the pressure has returned to normal, an effective dose of pure ergot alkaloids is administered, a fall in pressure results instead of the rise usually produced. Thus, histamine, in amounts frequently existing in ergot, is capable of reversing the effect of the ergot alkaloids. This is illustrated in Plate XIV, which shows the rise in blood pressure produced by a fluidextract containing practically no active amines, and in Plate XV, which shows the effect produced by the same preparation after a dose of aqueous extract of ergot had been given. The same observations have been duplicated by administering pure histamine before ergotamine.

As histamine and other amines have been found to exist in varying proportions in most of the samples of crude ergot entering this country (41), this method cannot be depended upon to accurately determine either the amine or alkaloidal content of Fluidextracts of Ergot because of the antagonistic manifestation of their effects upon blood pressure.

The assay of crude ergot necessitates the application of a method to a freshly prepared fluidextract. Such a preparation has been found to contain practically all of the amines and alkaloids present in the parent drug. Pressor methods are therefore contra-indicated in this connection.

Although aging of fluidextracts causes a rapid loss of amine activity, thereby eliminating the greater part of the interference in several months, pressor methods cannot be regarded as being nearly as accurate or as applicable as the Isolated Rabbit Uterus Method or the Cock's Comb Method, because of the great variations observed in test animals and the diminishing pressor response produced by repeated dosage. The effects produced by the first dose are often all that may be considered as significant.

Pressor studies, however, are exceedingly valuable in determining the presence or absence of amines, or the qualitative nature of ergot preparations, because of the characteristic differences in reaction produced by the amines and the alkaloids.

(*To be continued*)

GLEDITSCHIA TRIACANTHOS LINNÉ.*—A PRELIMINARY REPORT ON THE CHEMISTRY OF THE FRUIT.

BY LOYD E. HARRIS.

This plant, commonly known as Honey Locust, probably first came into prominence in 1878, when Lautenbach[1] reported the presence of an alkaloid which he called gleditschine.

* Read by title, Scientific Section, A. PH. A., Rapid City meeting, 1929.

[1] *Phila. Med. Times*, 1878 ("U. S. Disp.," 20, page 1410).

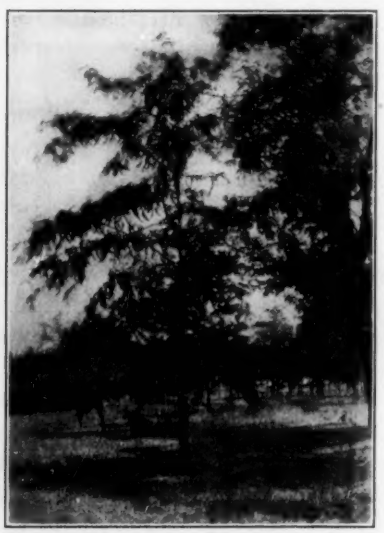
Goodman[1] *et al.*, in 1887, claimed to have extracted an alkaloid, stenocarpine, which had local anesthetic properties. Later investigators[2] failed to find this alkaloid. Plugge and Rauwerda[3] reported that the plant did not contain cystisine.

The fruit was studied in 1893 by Heckel and Schlagdenhauffen.[4] The composition reported by them is as follows:

Wax	0.625
Glucose and saccharose	37.650
Gum, pectin and tannin	23.993
Albuminous matter	8.300
Lignin and cellulose	20.427
Salts	9.005

EXPERIMENTAL.

For the purpose of this investigation, the seed pods were collected from two small trees. A total of fifty pounds of this material was obtained, from which 1850 Gm. of seed were separated.



Gleditschia Triacanthos L. A tree grown on campus of University of Oklahoma.

The seed was ground in a drug mill and 1830 Gm. of it were extracted with alcohol. A total of 169.5 Gm. of material was obtained, which was dark brown in color. This represented 9.25 per cent of the weight of the seed.

In order to separate the fixed oil from the above extractive, the mass was shaken repeatedly with successive portions of petroleum ether; 58.5 Gm., or 3.19 per cent of the weight of seed, of a light brown oil were obtained.

Gleditschia Triacanthos L. A limb of tree above, showing fruit.

The following constants of the oil were determined: S. V. 155.2, I. V. (Hanus) 93.9, n/D 23° 1.4685, Sp. gr. at 25°, 0.9336.

The oil was next saponified with alcoholic solution of potassium hydroxide. The alcohol was removed by

[1] *Med. Record* ("U. S. Disp.," 20, page 1410).

[2] F. W. Thompson, *Med. Age;* T. G. Novy, *Ph. Rundsch.;* John Marshall, *Phila. Med. News* (U. S. Disp., 20, page 1410).

[3] *Arch. Pharm.*, 234, p. 685.

[4] *Répert. pharm.* ("Yearbook of Pharmacy," page 156).

evaporation and then an aqueous solution prepared. The fatty acids were liberated by the addition of dilute hydrochloric acid.

A portion of the fatty acids thus obtained were then separated, as nearly as possible, into the liquid and solid fractions, by use of the Gusserow-Varentrapp method as given by Lewkowitsch.[1]

The bromide addition products of the unsaturated acids were prepared.[2] The absence of Linolenic acids was indicated by the failure to obtain the insoluble brominated products. Only a petroleum ether-soluble paste-like material was formed, which indicated the presence of oleic acid. This was confirmed by making a bromine determination by the method of Stepinow.[3] A value of 34.98 per cent was obtained while the theoretical amount is 36.14 per cent.

The presence of palmitic and stearic acids was indicated by the melting point of the recrystallized acids. After repeated purifications, a melting point of 56.6° C. (unc.) was obtained. The neutralization equivalent was found to be 208.9, as compared to the neutralization equivalent[4] of 197.5 for stearic acid and of 219.1 for palmitic acid.

SEED PODS.

After the seed had been removed from the pods, the material left was allowed to dry. It was ground by use of a drug mill and then extracted with petroleum ether. Only a small amount of extractive was obtained.

The petroleum-ether extract was brownish green in color. On evaporation of the solvent a greenish material separated, and on complete evaporation, extracting once with petroleum ether, a soft wax-like substance was obtained on the filter paper. This material was tested for solubility with the following results:

Ether, insoluble with yellowish green color.
Alcohol (same as ether), soluble in hot.
Chloroform, soluble.
Ethyl acetate, insoluble with yellowish green color, insoluble in hot.
Methyl alcohol (same as alcohol).

After recrystallization from alcohol, the compound melted at 69.2° C.

Alcoholic Extract.—Nineteen hundred and twenty-eight grams of the above material were extracted with alcohol; 274 Gm. of a thick, dark brown extract were obtained.

Solubilities.—Slightly soluble in water, muddy-like mixture; slightly soluble in water and alcohol, excess settled out in fine particles; insoluble in carbon tetrachloride, acetone and ethyl acetate.

The writer hopes to be able to study further the extractives from the seed-pod material, in the near future.

LABORATORY SCHOOL OF PHARMACY,
UNIVERSITY OF OKLAHOMA.

[1] Lewkowitsch, "Technology of Oils, Fats and Waxes," 6th ed., 1 (1921), 574.
[2] *Ibid.*, page 581.
[3] Kamm, "Qualitative Organic Analysis" (1923), 168.
[4] "Lewkowitsch," 6th ed., 1, 524.

See that your Railroad agent has all necessary information on Baltimore and Washington meetings in May.

PHYTOCHEMICAL NOTES.*

No. 104. The Inorganic Constituents of Echinacea.

BY S. H. CULTER.†

While engaged in the chemical study of *Echinacea*, the precipitation method of the so-called simple bases by means of phosphotungstic acid was tried out as directed.[1] Having used 1500 Gm. of the reagent, the precipitation seemed to continue indefinitely, yet the precipitate, when worked up according to the conventional method, yielded no organic base, although the extractive from 100 lbs. of drug had been used.

Inasmuch as phosphotungstic acid forms an insoluble potassium salt, it seemed desirable to ascertain the amount present of this element. It was possible that because so much drug was being worked on, its potassium content interfered with the reagent as a precipitant of the organic bases. While making this determination, it seemed best to make a quantitative determination of other inorganic constituents as well.

Approximately 100 Gm. of the crude drug were heated until vapors ceased to be given off. The charred mass was lixiviated with boiling water after having been transferred to a filter. The filtrate, amounting to about $1^1/_2$ liters, was evaporated to dryness, leaving a brown-colored residue which constituted the water-soluble ash. The portion remaining on the filter was now heated to a higher temperature until all the carbon was burned leaving a grayish white ash which constituted the water-insoluble ash.

The water-soluble ash was analyzed for potassium by precipitation with $HClO_4$ in the presence of 96 p. c. alcohol,[2] after the sulphates had first been removed and determined by precipitation with $BaCl_2$ as given in the procedure.

The carbonates were determined by titration with $N/10$ H_2SO_4. Using the same sample after titration, the chlorides were precipitated with $AgNO_3$ in the presence of HNO_3.[3]

The water-insoluble ash was treated with 10 p. c. HCl and filtered as described under the "Procedure for the Determination of Calcium."[4] The insoluble residue was ignited to constant weight and weighed as SiO_2. The filtrate was analyzed for calcium by precipitation with ammonium oxalate and ignition to CaO. The magnesium remaining in solution was precipitated with sodium ammonium phosphate[5] and ignited to $Mg_2P_2O_7$.

During the analysis for calcium, when the solution was treated with NH_4OH, a reddish brown precipitate resulted. It was filtered off, ignited to constant weight and the iron content determined by titration with $N/10$ $KMnO_4$.[6] The difference between the total weight and the weight of iron thus determined was calculated as aluminum.

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* From the laboratory of Edward Kremers.

† Lloyd Fellow 1928–1929.

[1] Barger, "The Simpler Natural Bases," page 118.

[2] G. N. Smith, "Quantitative Chemical Analysis," pages 68–69.

[3] *Ibid.*, page 55.

[4] *Ibid.*, page 75.

[5] *Ibid.*, page 79. [6] *Ibid.*, page 134.

In order that the percentage of the various constituents found could be calculated on the basis of the total ash and crude drug, it was necessary to carry out an analysis on a small sample. The water-soluble, acid-soluble, water-insoluble and acid-insoluble ash were determined by treatment similar to that of the larger quantity which was used for analysis. The results of the several determinations are herewith tabulated:

		Average.
Total ash	7.76 p. c. 7.72 p. c.	7.74 p. c.
Water-soluble ash	1.88 p. c. 1.82 p. c.	1.85 p. c.
Water-insoluble ash	5.88 p. c. 5.90 p. c.	5.89 p. c.
Acid-insoluble ash	3.21 p. c. 3.11 p. c.	3.16 p. c.
Acid-soluble ash (by difference)		4.58 p. c.

ANALYSIS OF WATER-SOLUBLE ASH.

Ion.	Percentage with reference to. Water-soluble ash.		Total ash.	Crude drug.
K	16.81 17.14	16.97 p. c.	4.05 p. c.	0.314 p. c.
SO_4	13.12 13.39	13.26 p. c.	3.17 p. c.	0.245 p. c.
CO_3	37.86 38.92	38.39 p. c.	9.17 p. c.	0.710 p. c.
Cl	4.04 4.17	4.10 p. c.	0.98 p. c.	0.076 p. c.

ANALYSIS OF WATER-INSOLUBLE ASH.

Ion.	Percentage with reference to. Water-insol. ash.		Total ash.	Crude drug.
Ca	13.50 12.88	13.19 p. c.	10.03 p. c.	0.776 p. c.
Mg	1.98 2.02	2.00 p. c.	1.52 p. c.	0.117 p. c.
SiO_3	26.29 26.14	26.21 p. c.	19.95 p. c.	1.543 p. c.
Fe'''	0.747 0.907	0.827 p. c.	0.628 p. c.	0.048 p. c.
Al	2.30 2.08	2.19 p. c.	1.66 p. c.	1.29 p. c.

From the data tabulated above, it becomes apparent that the extract from 100 lb. of crude drug contains 142.5 Gm. of potassium which would require 4109.5 Gm. phosphotungstic acid for precipitation.

BILL FAVORS NATIONAL ANTHEM.

A sub-committee of the House Committee on Judiciary February 4th voted to make a favorable report to the Committee February 5th on a bill (H. R. 14), which would make the "Star Spangled Banner" the national anthem of the United States. The bill, however, as the subcommittee voted to report it to the Committee reads as follows: "That the composition, consisting of the words and music known as the "Star-Spangled Banner," is designated the national anthem of the United States." This wording was taken from the Army and Navy regulations of 1914 and was adopted by President Wilson. The anthem was composed by Francis Scott Key during the bombardment of Fort McHenry.

THE STANDARDIZATION AND STABILIZATION OF VERATRUM PREPARATIONS AND THE HYDROGEN-ION CONCENTRATION FACTOR.—PAPER VI.*

BY E. E. SWANSON AND C. C. HARGREAVES.

I. Introduction. *III. Discussion.*
II. Experimental Data. *IV. Conclusions.*

I. INTRODUCTION.

In a number of previous articles (1, 2, 3, 4) the standardization and stabilization of aconite, nux vomica, gelsemium and veratrum preparations were reported. These reports include the study of a bio-assay method; the deterioration of preparations of aconite; the unreliability of the chemical method; the prevention of deterioration; the cause of deterioration or hydrolysis of the aconitine alkaloid into the less potent alkaloids, benzylaconine and aconine; and, finally, the hydrogen-ion concentration, which was shown to control the deterioration and stabilization. Swanson and Hargreaves (4) further reported that inasmuch as it was found that the above factors control the value of aconite preparations, other drug preparations were studied with the thought that possibly other fluidextracts and tinctures have a hydrogen-ion concentration or p_H value that might control their deterioration and stabilization. The drugs or fluidextracts of drugs that were studied are: Fluidextracts of Nux Vomica U. S. P. IX, Gelsemium U. S. P. IX and Veratrum U. S. P. IX.

It was found that the fluidextract of Nux Vomica U. S. P. IX is stable and does not require a definite hydrogen-ion concentration to control its potency; it does not deteriorate; the chemical method and bio-assay method gave correlative results. Fluidextracts of Gelsemium U. S. P. IX require no definite hydrogen-ion concentration to stabilize its alkaloids; the chemical method is unreliable; and this preparation should be assayed biologically.

The fluidextract of Veratrum U. S. P. IX seems to require some definite hydrogen-ion concentration to control its deterioration and stabilization. The chemical method is unreliable; this drug should be assayed biologically.

This report represents a more extensive study of the hydrogen-ion concentration factor in regard to the deterioration and stabilization of fluidextracts and tinctures of Veratrum U. S. P. IX. The chemistry of veratrum alkaloids has been studied by Eden (5). The pharmacological action has been reported by Pilcher and Sollman (6). The chemical assay of veratrum alkaloids, as found by several authorities, is not an indication of its therapeutic value. Houghton and Hamilton (7), reported the assay of a Veratrum preparation on frogs; later, Pilcher (8), reported a bio-assay method on frogs; and, still more recently, Rowe (9), described the use of mice as a bio-assay method.

II. EXPERIMENTAL DATA.

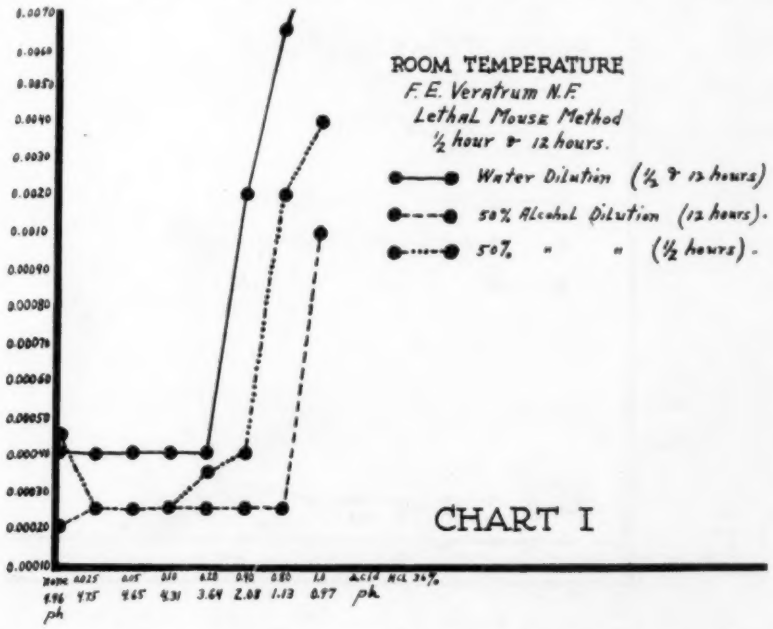
Two fluidextracts and one tincture of Veratrum were prepared. These preparations were so divided as to represent eight, ten or eleven samples. These samples received either no acid or different amounts of HCl 36% C.P. Each

* Scientific Section, A. PH. A., Rapid City meeting, 1929.

sample was assayed by the White Mouse Method as reported by Rowe, together with one-half-hour and twelve-hour lethal dose readings. Dilutions were made with distilled water and 50% alcohol. The hydrogen-ion concentrations were determined by the electrometric method. The difficulties in these determinations may be overcome by a method reported by Caldwell (10). Some of the samples were kept in an oven at 40° to 50° C. for seven months.

EXPLANATION OF TABLES.

Table I represents a fluidextract of Veratrum U. S. P. IX, made February 3, 1927, divided into eight parts. To seven of these were added various amounts of HCl 36%. All samples were kept at room temperature and exposed to light. The original assay was 0.00035 Gm. per



Gm. of mouse; they were all assayed again March 15, 1929, by the Lethal Mouse Method and one-half-hour and 12-hour readings were taken. Dilutions were made with distilled water and 50% alcohol. The hydrogen-ion concentrations were determined by the electrometric method.

TABLE I.—FLUIDEXTRACT OF VERATRUM U. S. P. IX. KEPT AT ROOM TEMPERATURE. MADE IN 2-3-27. TESTED 3-15-29. ORIGINAL ASSAY = 0.00040 GM. PER GM. (MOUSE). STANDARD DOSE = 0.00025 GM. PER GM. (MOUSE).

Sample number.	Am't. of 36% HCl in 100 cc.	p_H.	M. L. D. ½ hr. dose per Gm. H_2O.	M. L. D. 12 hrs. dose per Gm. H_2O.	M. L. D. ½ hr. dose per Gm. 50% alcohol.	M. L. D. 12 hrs. dose per Gm. 50% alcohol.	Bio-assay ½ hr. H_2O per cent.	Bio-assay ½ hr. 50% alcohol per cent.	Bio-assay 12 hrs. 50% alcohol, per cent.	Chemical assay per cent.
1	1%	0.97	0.0080	0.0080	0.0040	0.0010	3%	6.25%	25%	1.065%
2	0.8%	1.13	0.0065	0.0065	0.0020	0.0020	3.85%	12.5%	12.5%	.....
3	0.4%	2.08	0.0020	0.0020	0.00040	0.00025	12.5%	62.5%	100%	.....
4	0.2%	3.64	0.00040	0.00040	0.00035	0.00025	62.5%	71%	100%	.....
5	0.10%	4.31	0.00040	0.00040	0.00025	0.00025	62.5%	100%	100%	.....
6	0.05%	4.65	0.00040	0.00040	0.00025	0.00025	62.5%	100%	100%	.....
7	0.025%	4.75	0.00040	0.00040	0.00025	0.00025	62.5%	100%	100%	.....
8	None	4.96	0.00040	0.00040	0.00045	0.00025	62.5%	55%	100%	1.047%

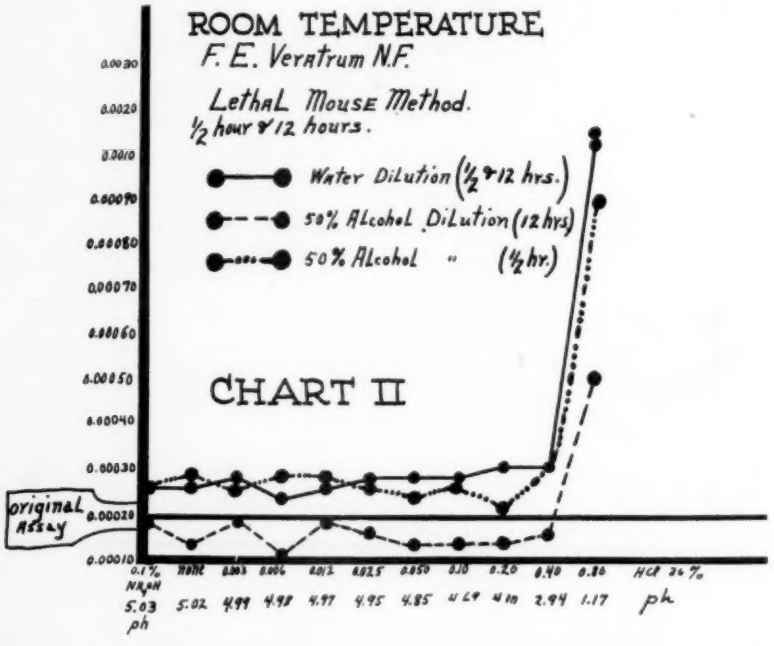
III. DISCUSSION.

The data in Table I show that this fluidextract of Veratrum U. S. P. IX maintained its potency for over two years with a p_H of 4.96 to 3.64. With a p_H of 2.08, 1.13 and 0.97 there is

considerable deterioration, the deterioration increasing as the p_H increases. With distilled water dilutions, the lethal dose is the same after one-half-hour and twelve-hour periods. Fifty per cent alcohol, however, increases the toxicity of the preparation for both the one-half-hour and twelve-hour periods.

This preparation having a p_H of 4.96 required no acid for maintaining its potency. Acid could be added to the preparation without injury, until a p_H of 3.64 was reached, and too much acid decreased its activity.

Table II represents a fluidextract of Veratrum U. S. P. IX that was made February 24, 1928. It was divided into eleven parts; to nine of these samples various amounts of HCl 36% were added. To one of the samples 0.1% NH_4OH 40% was added. All samples were kept at room temperature and exposed to light. The original assay was 0.00020 Gm. per Gm. of mouse. They were all assayed again May 20, 1929, by the Lethal Mouse Method. One-half-hour and



twelve-hour readings were taken. Solutions were made with distilled water and 50% alcohol. The hydrogen-ion concentrations were determined by the electrometric method.

TABLE II.—FLUIDEXTRACT OF VERATRUM N. F. KEPT AT ROOM TEMPERATURE. MADE IN 2-24-28. TESTED 5-20-29. ORIGINAL ASSAY = 0.00020 GM. PER GM. (MOUSE).

Sample number.	Am't. of 36% HCl in 100 cc.	p_H.	M. L. D. ½ hr. dose per Gm. H_2O.	M. L. D. 12 hrs. dose per Gm. H_2O.	M. L. D. ½ hr. dose per Gm. 50% alcohol.	M. L. D. 12 hrs. dose per Gm. 50% alcohol.	Bio-assay H_2O Per cent.	Bio-assay ½ hr. 50% alcohol per cent.	Bio-assay 12 hrs. 50% alcohol per cent.	Chemical assay
1	0.8%	1.17	0.00125	0.00125	0.00090	0.00050	20%	27.2%	50%	1.045
2	0.4%	2.94	0.00030	0.00030	0.000275	0.00015	83%	83%	166%	...
3	0.2%	4.10	0.000275	0.000275	0.00020	0.000125	91%	125%	200%	...
4	0.1%	4.69	0.000275	0.000275	0.00025	0.000125	91%	100%	200%	...
5	0.05%	4.85	0.000275	0.000275	0.000225	0.000125	91%	111%	200%	...
6	0.025%	4.95	0.00025	0.00025	0.00025	0.00015	100%	100%	166%	...
7	0.0125%	4.97	0.000225	0.000275	0.000275	0.000175	111%	83%	143%	...
8	0.0060%	4.98	0.000275	0.000275	0.000275	0.00010	91%	83%	250%	...
9	0.0030%	4.99	0.000250	0.000250	0.00025	0.000175	100%	100%	192%	...
10	None	5.02	0.000250	0.000250	0.000275	0.000125	100%	83%	200%	...
11	0.1% NH_4OH	5.03	0.000250	0.000250	0.00025	0.000125	100%	100%	200%	1.037

The data show that this fluidextract of Veratrum U. S. P. IX has not deteriorated. Dilutions made with 50% alcohol gave the same lethal dose as dilutions with distilled water in the one-half-hour period, but in the twelve-hour period or readings the toxicity increased below the original assay of the preparation.

This preparation required no acid to stabilize its activity. Acid could be added to the preparation without injury until a p_H of 4.10 was reached; too much acid decreased the activity. Dilutions made with distilled water and 50% alcohol gave correlative readings in one-half-hour periods. The toxicity of the preparation was increased by 50% alcohol dilutions during the twelve-hour period.

Table III treats of the same preparation as that of *Table II*. These samples, however, were kept at an incubation temperature of 50° C. and were not exposed to light for 7 months; the original assay before incubation was 0.00020 Gm. per Gm. of mouse. These samples were again assayed May 25, 1929, by the Lethal Mouse Method. One-half-hour and twelve-hour readings

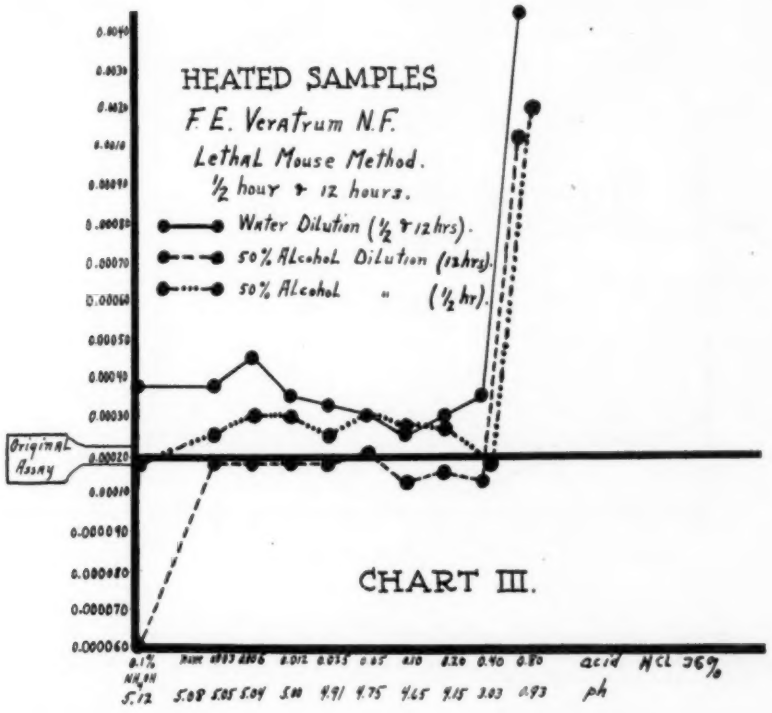


TABLE III.—FLUIDEXTRACT OF VERATRUM N. F. HEATED SAMPLES. MADE IN 2–24–28. TESTED 5–25–29. ORIGINAL ASSAY = 0.00020 GM. PER GM. (MOUSE). STANDARD M. L. D. = 0.00025 GM. PER GM. (MOUSE).

Sample number.	Am't. of 36% HCl in 100 cc.	p_H.	M. L. D. ½ hr. dose per Gm. H_2O.	M. L. D. 12 hrs. dose per Gm. H_2O.	M. L. D. ½ hr. dose per Gm. 50% alcohol.	M. L. D. 12 hrs. dose per Gm. 50% alcohol.	Bio-assay ½ hr. H_2O. per cent.	Bio-assay ½ hr. 50% alcohol per cent.	Bio-assay 12 hrs. 50% alcohol per cent.	Chemical assay, per cent.
1	0.8%	0.93	0.0045	0.0045	0.0020	0.00125	5.5%	12.5%	20%	1.045
2	0.4%	3.03	0.0035	0.0035	0.000175	0.000125	7%	1.42%	200%	...
3	0.2%	4.15	0.00030	0.00030	0.000275	0.00015	83%	91%	166%	...
4	0.10%	4.65	0.00025	0.00025	0.000275	0.000125	100%	91%	200%	...
5	0.05%	4.91	0.00030	0.00030	0.00030	0.00020	83%	83%	125%	...
6	0.025%	5.00	0.000325	0.000325	0.00025	0.000175	77%	100%	143%	...
7	0.0125%	5.04	0.00035	0.00035	0.00030	0.000175	71.5%	83%	143%	...
8	0.0060%	5.05	0.00035	0.00035	0.00030	0.000175	71.5%	83%	143%	...
9	0.0030%	5.08	0.000375	0.000375	0.00025	0.000175	66.6%	100%	143%	...
10	0.1% NH_4OH	5.12	0.000375	0.000375	0.000170	0.000060	66.6%	147%	417%	1.037

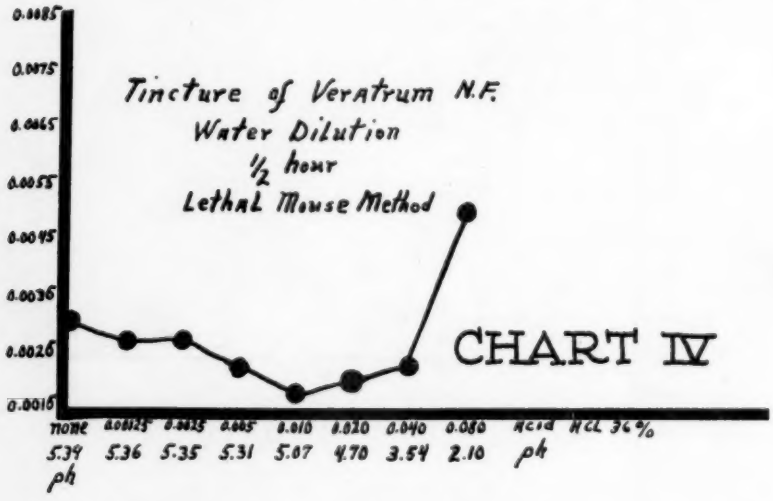
were taken. Dilutions were made with distilled water and 50% alcohol. The hydrogen-ion concentrations were determined by the electrometric method.

The data show that during the incubation period this preparation deteriorated more than did the preparations kept at room temperature. Sample No. 4 has the same potency as several of the most active samples in Table II. Dilutions with distilled water gave the same readings in the one-half-hour and twelve-hour periods. Fifty per cent alcohol dilutions in the one-half hour-period gave a higher potency than did the distilled water dilutions; 50% alcohol dilutions in the twelve-hour period show an increase in activity over the original assay.

Sample No. 10, containing NH_4OH, shows a toxicity of 0.000060 Gm. per Gm. of mouse in the twelve-hour period—a great increase in toxicity.

These samples, particularly the alcohol dilutions show considerable variation in activity. A p_H of 4.64 seems to stabilize the preparation equal to the preparation in Table II.

Table IV represents a tincture of Veratrum U. S. P. IX that was made February 27, 1928. This preparation was divided into eight parts; various amounts of HCl 36% were added. The samples were kept at an incubation temperature of 50° C. and were not exposed to light for seven months. The original assay was 0.0018 Gm. per Gm. weight of mouse. These samples were assayed again April 9, 1929. One-half-hour and twelve-hour lethal dose readings were taken.



Dilutions were made with distilled water. The hydrogen-ion concentrations were determined by the electrometric method.

TABLE IV.—TINCTURE OF VERATRUM N. F. HEATED SAMPLES (7 MONTHS). ORIGINAL ASSAY = 0.0018 GM. PER GM. (MOUSE). (TINCTURE MADE 2-27-28). TESTED 4-9-29.

Sample number.	Am't. of 36% HCl 100 cc.	p_H.	M. L. D. ½ hr. H_2O.	M. L. D. 12 hrs. H_2O.	Bio-assay per cent.	Chemical assay.
1	0.080%	2.10	0.0050	0.0050	50%	0.105
2	0.040%	3.54	0.00275	0.00275	91%	...
3	0.020%	4.70	0.0020	0.0020	125%	...
4	0.010%	5.07	0.00175	0.00175	143%	...
5	0.005%	5.31	0.00225	0.00225	111%	...
6	0.0025%	5.35	0.00275	0.00275	91%	...
7	0.00125%	5.36	0.00275	0.00275	91%	...
8	None	5.39	0.0030	0.0030	83%	0.108

The data show that with a p_H of 5.07, Sample No. 4 assays 0.00175. The original assay being 0.0018, there was no deterioration when kept in a temperature of 50° C. for seven months.

According to the data this method of assaying Veratrum preparations suggests that a distilled water dilution gives more consistent readings than does an alcoholic dilution. The alcoholic dilutions show an increase in toxicity in the one-half-hour period and a still greater increase in toxicity after the twelve-hour period, whereas the distilled water dilution gave the same toxicity in both the one-half-hour and twelve-hour periods. The alcoholic dilutions, after the twelve-hour period or readings, show a greater toxicity of the preparation than does the original assay. It is recommended, therefore, that Veratrum preparations be assayed by the Lethal Mouse Method which consists of an intraperitoneal injection of veratrum per Gm. wt. of mouse, 0.00025 Gm. per Gm. of mouse for the drug, and fluidextract and 0.0025 Gm. per Gm. of mouse for the Tincture, dilutions to be made with distilled water and one-half-hour readings observed as the lethal period. The hydrogen-ion concentration factor or p_H values of 5.00 to 4.65 in the fluidextract and tincture of veratrum seem to stabilize its active principles. This is observed more accurately in the heated samples (*Tables II and IV*) and (*Charts II and IV*). The heated samples show the value of the hydrogen-ion concentration factor in stabilizing veratrum preparations. The tincture (*Table IV and Chart IV*) has a greater p_H range and shows that Sample No. 4, with a p_H of 5.07 seems to be about equal to the original assay. The stability of veratrum preparations, rapidly decreases with lessening values of p_H. The active principles of aconite, nux vomica and gelsemium are not injured by increasing amounts of acid. Considering the similarity in pharmacological properties of veratrum and aconite, it is interesting to note that veratrum is easily injured by excessive amounts of acid, whereas aconite requires acid to prevent hydrolysis or deterioration. The above data seem to show that veratrum preparations (the fluidextracts and tinctures) require a p_H of 4 to 5 to prevent deterioration or to stabilize their active principles.

IV. CONCLUSIONS.

1. Fluidextracts and tinctures of veratrum should be assayed biologically; the chemical method is unreliable.
2. Distilled water dilutions are more reliable than are the alcoholic dilutions.
3. It is evident that the hydrogen-ion concentration factor or p_H factor controls the active principles of veratrum.
4. A p_H value of 4 to 5 seems to stabilize these active principles.

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A COMMENDATION FOR PHARMACY.

"A word of commendation has long been due the profession, and the JOURNAL[1] will make the most of this opportunity to voice it. There is perhaps no more responsible servant of the people than the registered pharmacist. He is less adequately compensated than equally responsible servants in other fields. Upon his precise functioning so much depends. It is cause for gratification and for congratulation that an outstanding representative[2] of the profession in Texas should have been honored, as unexpectedly, as deservedly, with high recognition by the national organization."

[1] *Dallas Daily Evening Journal.* [2] Walter D. Adams elected *First Vice-President* of the A. PH. A.

CRITICAL REMARKS ON THE U. S. P. PANCREATIN ASSAY.*

BY. F. E. WILLSON.

The U. S. P. X included under Pancreatin an assay method for the determination of the tryptic activity.

This method is based upon the total disappearance of the substrate, casein, by the digestive action of the trypsin. To meet the U. S. P. requirements the directions state that at the end of the digestion period, upon the addition of three drops of a mixture of alcohol and acetic acid, no precipitate is produced. In other words, there should be no casein present—which can be thrown out of solution.

For routine analytical purposes a series of tubes are prepared to which varying amounts of the pancreatin solution are added. In this way the strength of the sample may be found without running several consecutive tests, if the sample is either above or below U. S. P. strength. The tube in the series next to the one in which precipitation first appears should, therefore, represent the tryptic strength of the sample under test.

In reading over the U. S. P. assay method it would seem that the end-point described would be quite definite. However, in actual practice this is not the case. There is a gradation in the appearance of the tubes from the perfectly clear to hazy, then to distinctly precipitated. The tube in which precipitation first takes place is very difficult to judge because of this gradual change. The tube in the series immediately after the clear ones, though hazy or even slightly cloudy in appearance, can hardly be recorded as precipitation. Because of this indefinite appearance of precipitation at the end of the test different observers will choose different tubes as the point at which precipitation takes place. This was proven to be the case when samples of pancreatin were submitted to a number of different laboratories for assay. The results obtained were far from concordant, especially in the case of samples two or three times the U. S. P. strength. It was attempted to trace these divergencies to the casein supply, but practically as divergent results were obtained using samples of the same lot of casein.

The suggestion has been made that a U. S. P. sample be chosen as a standard and unknown strength pancreatins be assayed, using this standard sample for comparison. Two series of tubes would, therefore, be compared and from the one representing 100% with the standard sample, the strength of the unknown would be determined. However, this seems as unsatisfactory as the present U. S. P. method, since to match appearances of two slightly cloudy or cloudy tubes is practically as difficult and as liable to variance in the hands of different operators as when the end-point is determined in the present U. S. P. method.

It would, therefore, seem desirable that in the next revision of the Pharmacopœia that either a totally new method be adopted or such modifications in the present method be made that more consistent results may be obtained.

The assay method for the determination of the amylolytic activity of pancreatin in the present Pharmacopœia is for the most part quite satisfactory. There are, however, at least two points which seem worthy of consideration.

The method depends upon the absence of blue, red or violet color when a portion of the digested starch paste is added to dilute iodine solution.

* Scientific Section, A. PH. A., Rapid City meeting, 1929.

The first point in question in this method is whether or not the iodine solution should be shaken after the addition of the digested starch paste. It will be found that on carrying this method out as the end-point is approached the addition of the required amount of digested starch paste to the iodine solution will give a blue to violet color, and this color will remain dispersed through the solution. If the solution is now inverted several times to thoroughly mix, the blue color will totally disappear. With high strength samples of pancreatin this is particularly noticeable and whether or not the iodine solution is shaken has a considerable influence on the assay results.

I would recommend that in the next revision of the U. S. P. the method be so modified as to state definitely that the iodine solution be not shaken after the addition of the starch paste. In this way the point at which the starch totally disappears could be more accurately determined.

The second point of indefiniteness in the method is the temperature of the iodine solution. It has been observed that the color reaction between starch and dilute solutions of iodine is very sensitive to temperature; the lower the temperature the deeper is the color. It is possible to obtain a divergence in results on this point, which is shown by carrying out the following experiment:

Two tubes of iodine solution are prepared ready for the test; one is adjusted to a temperature of 20° C.; the other is brought to a temperature of 30° C. To these two tubes the required amounts of a starch paste digested by a U. S. P. pancreatin are added. A blue or violet color will be produced with the iodine solution at 20° C. while the one at 30° C. will usually show no color or possibly a very faint coloration. The color reaction can be brought out in the latter tube by cooling it down; the lower the temperature the deeper the color becomes. This shows that if approximately identical temperatures of the iodine solution were not observed some divergence in results would be obtained.

To overcome this possible source of inaccuracy in the test, it would be recommended that in the next revision the temperature of the iodine solution used in the test be definitely stated. A temperature of 23° C. has been found convenient in carrying out this method.

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THE ASSAY OF PANCREATIN.*

BY F. E. WILLSON.

Numerous methods have been suggested for the determination of the tryptic activity of pancreatin. The majority of these are impractical as routine laboratory methods either because of the indefiniteness of the end-point or the time required for carrying them out. Practically all such determinations are based upon the digestive action of trypsin on some weakly alkaline substrate, such as casein or egg albumin. Casein solutions have been favored because of the fact that the undigested casein remaining, after the digestion has been carried on for a definite length of time, can be easily thrown out of solution by the addition of a mixture of

* Scientific Section, A. PH. A., Rapid City meeting, 1929.

alcohol and acetic acid. However, the end-point in such determinations is very difficult to determine and the method is sensitive to conditions under which the test is run, thereby giving divergent results in the hands of different operators.

This is true both of methods in which the amount of digestion produced by a standard sample and of those which use the total disappearance of substrate as the end-point as a means of standardization. The latter has the added disadvantage that the last portions of the substrate are very slow in digesting, perhaps due to the decomposition products of digestion having an inhibiting action. Determinations based upon the peptonization of milk by trypsin as a means of standardization also give widely varying results, probably partly due to the condition of the milk.

In the search for a more accurate method Sorenson[1] suggested that his formol titration for amino acids be applied. This method is based upon the breaking down of the polypeptide linkages of a casein solution into carboxyl and amino acid groups by the trypsin. The amount of amino groups formed by the hydrolysis of the casein solution cannot be determined directly because of the amphoteric properties of the amino acid groups. This is overcome by the addition of a solution of formaldehyde which converts the amino groups into methyleneimino groups which allows the free carboxyl groups to be titrated by a standardized alkali solution.

This method was further improved upon by Smith[2] for use as a laboratory method for determination for the tryptic activity of pancreatin. However, it was found that some changes could be made in his method that would make the method more accurate and rapid. Following is an outline of the method as now followed:

SOLUTIONS REQUIRED.

A. A 4% casein solution (Hammerstein's casein as supplied by Merck) adjusted to neutrality by the addition of *N*/1 sodium hydroxide, phenolphthalein being used as an outside indicator.

B. A 40% formaldehyde solution to which 1 cc. of a 0.5% phenolphthalein solution in 50% alcohol has been added. This solution is brought to neutrality with *N*/1 sodium hydroxide.

C. A 1% unfiltered pancreatin solution in distilled water.

METHOD.

The casein solution and a supply of recently boiled distilled water is heated to 55° C. Then 24 cc. of the distilled water is added to 25 cc. of the casein solution and placed in a water-bath at 55° C. At the same time 25 cc. of the distilled water is added to 25 cc. of the casein solution in another flask or tube and also heated to 55° C. This is to be used as a blank. Add 1 cc. of the pancreatin solution to the first casein and water mixture, mix, and allow to digest for exactly 20 minutes at 55° C. At the end of this time 20 cc. are withdrawn and placed in a 50-cc. Nessler tube and 10 cc. of the formaldehyde solution (Solution B) added, mixed well and then titrated with *N*/10 sodium hydroxide to bring the solution to the same pink color as a previously titrated blank.

While the digestion is proceeding the blank test can be titrated by withdrawing 20 cc. of the solution, to which no pancreatin has been added, treating with 10 cc. of Solution B and titrating with *N*/10 sodium hydroxide, noting the number of cc. required.

To compute the strength of the pancreatin the number of cc. of *N*/10 sodium hydroxide used in the blank is subtracted from the number of cc. used in titrating the digested sample. Multiply the number of cc. thus obtained by 100 and the result will be the percentage strength of the tryptic activity.

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[1] S. P. Sorenson, "Études enzymatiques," *Comp. rend. du Carlsberg*, 7 (1907).

[2] A. R. Smith, "The Measurement of Relative Tryptic Activity," *Pharm. J.*, 35 (1912), 137.

This method of determination was arrived at after numerous samples had been subjected to the test, which had been previously assayed and reassayed, according to the U. S. P. method. At first $N/5$ sodium hydroxide was used in the final titration. It was found that pancreatin samples assaying U. S. P. or 100% invariably required 0.5 cc. of $N/5$ alkali after the blank had been subtracted. Therefore, it was decided to accept 0.5 cc. of $N/5$ NaOH as representing 100% tryptic activity. This standard was found to apply equally well in higher strength pancreatin samples. For instance, a sample assaying 300% by the U. S. P. method required 1.5 cc. of $N/5$ NaOH. In order to increase the accuracy of the method $N/10$ NaOH was used and results checked against those obtained with $N/5$ NaOH. It was found that the accuracy was increased and it had the added advantage that the strength can be determined directly by multiplication of the cc. by 100.

The actual test requires little discussion as it is quite simple in manipulation. Some difficulty might be found when carrying this test out for the first time in the preparation of the casein solution. Smith's method is followed rather closely in this respect. To prepare a liter of solution, 40 Gm. of casein is added to 900 cc. of recently boiled distilled water to which approximately 25 cc. of $N/1$ sodium hydroxide has been added. The casein is brought into solution by stirring or mixing from time to time. If at the end of an hour or two all the casein is not dissolved a few more cc. of $N/1$ alkali are added so as to accomplish this. After all the casein has been dissolved, it is usually necessary to add a few more cc. of $N/1$ NaOH to bring the solution to neutrality or a very faint pink color, using phenolphthalein as an outside indicator. Then 5 cc. of chloroform are added as a preservative and the volume made up to one liter. The casein solution is now ready for use and will keep for several months, providing it is saturated with chloroform.

A number of laboratories using the method as outlined ($N/5$ alkali was used in the titration) were able to obtain fairly concordant results. The results varied no more than the results obtained using the U. S. P. test and the method had the disadvantage of being unfamiliar to practically all the investigators. It was suggested that possibly these divergencies were due partly to the adjustment of the casein solution and some evidence was brought out to substantiate this claim. In order to find out whether or not this were true, it was decided to carry out the test using casein solutions of varying hydrogen-ion concentrations. In order to do this a large volume of casein solution was prepared using only enough alkali to completely bring the casein into solution. This solution was divided into portions and each portion brought to different hydrogen-ion concentrations with alkali. The Hellige hydrogen-ion comparator was used for determination of the p_H values of the various solutions.

Four samples of powdered pancreatin were selected for study of which the tryptic activity had been checked and re-checked by the U. S. P. casein method. According to the U. S. P. test the samples gave the following assays:

1. 80%; 2. 125%; 3. 350%; 4. 325%.

The outlined method was then applied, using the casein solutions of varying hydrogen-ion concentrations.

In the following table the results obtained are tabulated. The p_H values and the percentage strengths obtained on assay are recorded.

	p_H* 6.9.	p_H* 7.5.	p_H† 7.9.	p_H† 8.4.	p_H† 8.9.	p_H† 9.1.	p_H† 9.4.
Sample 1	78%	85%	79%	68%	66%	59%	52%
Sample 2	121%	124%	123%	113%	103%	79%	76%
Sample 3	362%	363%	350%	335%	332%	307%	290%
Sample 4	350%	353%	334%	326%	328%	299%	271%

* Casein solution p_H value determined using brom-thymol blue color disc in comparator.

† Casein solution p_H value determined using thymol blue color disc (alkaline range) in comparator.

The results obtained indicate clearly that the hydrogen-ion concentration of the casein solution must be taken into consideration in carrying out this method in order to insure consistent results. Data obtained indicate that a preference is shown for casein solutions with a p_H value of 7.5. However, pancreatin samples assayed using casein solutions with p_H values of 6.9 and 7.9 show little variance from the results obtained with the former casein solution mentioned. We would, therefore, suggest that the casein solution for use in this method be adjusted to a p_H value not less than 7.0 and not more than 8.0.

The advantages of this method over the present U. S. P. method are:

(*a*) A definite end-point is obtained.

(*b*) It is much shorter, providing a supply of the preserved casein solution is kept on hand.

(*c*) More consistent results can be obtained, especially with the higher strength samples of pancreatin.

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ACCELERATED PRODUCTION OF SPECIFIC URINARY PIGMENTS BY DRUG ADMINISTRATION.*

I. EFFECT OF PHENYLDIMETHYLPYRAZOLON ON UROBILIN FORMATION.

BY FREDERICK G. GERMUTH.

INTRODUCTION.

The relation of chemical constitution to physiological activity in synthetic therapeutic agents has long been a subject of fascinating interest. Aside from purely theoretical aspects, the action of chemical agents upon the animal organism, and upon mankind in particular, is avowedly of the greatest importance. A knowledge of the relationship obtaining is of fundamental significance and importance—not alone to those contemplating the exploration of this vast field, but is certainly of no less import to the practitioner whose duty it is to prescribe the employment of this particular class of medicinal substances. It is believed, therefore, that the paper here presented—the first of a contemplated series dealing with urinary pigment formation engendered by the administration of specific organic medicinals—will be of interest alike to the members of the medical and pharmaceutical professions as well as to the chemist and others engaged in scientific work.

In a previous research,[1] the author has furnished data describing the pro-

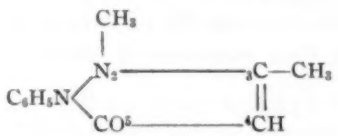
* Contribution from the Division of Research, Bureau of Standards, City of Baltimore.

[1] Germuth, *American J. Pharm.*, 99 (1927), No. 11.

nounced action of the sulphone, diethylsulphonemethylethylmethane (Trional) upon the production of the pigment, hæmatoporphyrin. This was followed by a paper dealing with the accelerating effect of the most therapeutically active member of this series of alkylated soporifics, diethylsulphonediethylemethane (Tetronal), upon the porphyrin, in which attention was accorded the fact that an increase in ethyl groups in the molecular structure of this aliphatic compound imparts, in addition to a high degree of therapeutic activity, properties which result in the formation in the system of a proportionately greater amount of hæmatoporphyrin than that observed when either sulphonal or trional is ingested.[1] This work prompted the desire to instigate further investigations of like character in the effort to ascertain the ultimate effect of certain compounds upon the production of physiological bodies of known, definite srructure.

HISTORICAL.

It will be recalled that the constitution which Knorr[2] first ascribed to a tetrahydroquinoline derivative was the cause for testing the so-called dimethyloxyquinizine, the antipyretic effect of which was found to be most pronounced.[3] At a later period this compound was recognized as phenyldimethylpyrazolon,[4] better known at present, perhaps, as antipyrine—possessing the structural formula:



While Michaelis[5] affirms that another formula may also be ascribed to this compound, that given is considered as more correctly embodying the chemical constitution of phenyldimethylpyrazolon.

It may be of interest to observe at this place that, while antipyrine was once widely prescribed in conjunction with sodium bromide in the treatment of disorders of nervous origin (its anæsthetic action on nerve endings rendering its application rather desirable in these conditions), its employment in this respect has been considerably curtailed by the advent of derivatives, such as 4-dimethylaminoantipyrine (Pyramidon), Pyrosal and certain others in which alkylation of the nitrogen has taken place.

METHOD.

The method of Hoppe-Seyler[6] was applied in the estimation of urobilin in the samples of normal and pathological urines under examination, insuring, it is believed, a high degree of accuracy. The essential procedure is as follows:

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[1] Germuth, *Indian Med. Gaz.*, 64 (1929), No. 9.
[2] Knorr, *Ber.*, 17 (1884), 546, 2032.
[3] Filehne, *Z. klin. Med.*, 7 (1884), 6.
[4] Knorr, *Ann. Chim.*, 238 (1887), 137.
[5] Michaelis, *Ibid.*, 320 (1902), 1.
[6] Hoppe-Seyler, *Virchow's Arch.*, 124.

One hundred ml. of urine are acidified with 1:4 H_2SO_4, and then saturated with $(NH_4)_2SO_4$. After one hour has elapsed, the precipitate is collected on a filter, washed with a saturated solution of $(NH_4)_2SO_4$, and repeatedly extracted with a solution consisting of equal portions of C_2H_5OH and $CHCl_3$, after pressing firmly. The filtered solution is treated with H_2O in a separatory funnel until the $CHCl_3$ separates well and becomes clear. The $CHCl_3$ solution is evaporated on the water-bath in a weighed beaker, the residue dried at 100° C., and then extracted with $(C_2H_5)_2O$. The ethereal extract is filtered, the residue on the filter dissolved in C_2H_5OH, and transferred to the beaker and evaporated; then carefully dried and weighed.

EXPERIMENTAL.

Recognition was accorded the fact that the urinary pigment here considered is present in increased quantities in disorders accompanied by fever; in cardiac diseases, atrophic cirrhosis of the liver, and certain other physiological conditions. Adequate precaution was taken to obviate any discrepancies that might accrue as a result of the presence of factors that might tend to introduce errors in the experimental portion of this work.

Ten samples of urine, representing the 24-hour output of patients for whom the antipyretic had been prescribed, and to whom it had been administered in dosages of 15 grains per day, intermittently, for a period of ten days, were collected on the eleventh day. Ten additional samples, taken from patients whose hospitalization had not required the use of antipyrine, and who were, apparently, free of any disorder that might cause an increase in the production of urobilin, were collected and subjected to the same treatment given the physiological urines.

Table I furnishes the data obtained by careful analysis of the samples of normal body fluid.

TABLE I.—DETERMINATION OF UROBILIN IN NORMAL URINE.

Amount expressed in mg. per liter.

Sample No.	1	2	3	4	5	6	7	8	9	10
Quantity	45	34	38	29	45	33	78	42	37	49

Average—43 mg.

The ten samples of urine obtained from patients who had been given the antipyrine treatment were next submitted to chemical examination, and the results given in Table II observed.

TABLE II.—DETERMINATION OF UROBILIN IN PATHOLOGICAL URINE.

Amount expressed in mg. per liter.

Sample No.	1	2	3	4	5	6	7	8	9	10
Quantity	98	110	108	95	138	106	142*	89	104	126

Average—112 mg.

* Patient developed a decided icterus.

REMARKS.

Consideration of the results tabulated justify the belief that the continued employment of phenyldimethylpyrazolon over a period of ten days or less, promotes the disintegration of erythrocytes, causing a condition characterized by the appearance of excessive amounts of urobilin in the urine. While certain forms of disease also tend to emphasize this condition, the action of the synthetic appears to be most readily discerned. As will be shown in a later paper, acetanilid exerts a similar effect, but fails to act as quickly as the compound here considered.

While some degree of variation has been experienced in the different results, it is obvious that the samples of urine obtained from the physiological sources contain a marked excess of urobilin over that generally encountered in so-called normal urines.

SUMMARY.

(*1*) The administration of phenyldimethylpyrazolon over a certain period of time occasions the appearance of an abnormal quantity of urobilin in the system.

(*2*) It is believed that the disintegration of erythrocytes is considerably augmented by continued ingestion of the antipyretic, resulting in an increased proportion of the urinary pigment.

(*3*) Data are furnished, showing the relative amounts of the body existing in normal and physiological samples of urine.

(*4*) Future work on the effect of certain of other therapeutic agents upon urobilin production, is contemplated.

ACKNOWLEDGMENTS.

The author desires to acknowledge, with thanks, the coöperation extended him by Harry Goldsmith, M.D., physician-in-chief, Psycopathic Department of Baltimore City Hospitals, from whom a number of the samples of urine utilized in the tests were obtained, and the assistance rendered by Nelson T. Carey, M.D., of the staff of Mercy Hospital,[1] in furnishing samples of urine which were previously examined and employed for control purposes.

COMMENTS ON SOME TESTS AND ASSAYS OF THE U. S. P. X.*

BY HERBERT C. KASSNER.

For the past two years, part of my work has been to conduct a course of laboratory instruction for large classes of third year students, candidates for the degree of Pharmaceutical Chemist; part of the course consists in the carrying out of many U. S. P. tests and processes. It has been repeatedly made evident to me that certain tests and assays caused considerable difficulty and seemed in need of improvement; for example, on introducing impurities into certain substances, even in reasonably large proportions, it appeared impossible to detect them by the prescribed U. S. P. tests; again, some tests appeared to be unworkable unless modifications were made. It seemed advisable to call attention to the difficulties encountered and for this reason this paper has been written.

The list of subjects criticized does not pretend to be by any means comprehensive; it contains only those tests and assays which were included as a part of the course because of their importance from the educational point of view and which were the cause of trouble in one way or another. If a systematic search were made of the Pharmacopœia, doubtless many more difficulties on similar lines would be encountered.

All the tests commented upon have been carefully examined, many series of experiments being carried out and suggestions for modifications made wherever possible. In some cases it is merely the wording of the Pharmacopœia which has been

[1] At present on the Staff of Johns Hopkins Hospital.

* Scientific Section, A. PH. A., Rapid City meeting, 1930.

criticized, and alterations are recommended especially when ambiguities or contradictions are apparent.

The order in which the subject-matter has been arranged is that of the Pharmacopœia, page references being given in every case.

Acetylsalicylic Acid, p. 13.—In order that the melting point may be used as a standard, a maximum figure should be given in addition to the minimum of 132° stated in the U. S. P., which determines this in a bath previously heated to 120°. It has been suggested by Corfield and Self (*Pharm. Jour.*, 110 (1923) 361) that a melting point range of 133° to 138°, determined in the usual way, is advisable.

Alcohol, p. 39.—*Boiling point.* In the sentence "Alcohol is readily volatilized even at low temperatures and boils at about 78° C.," the first statement is redundant since the volatile character of alcohol has already been mentioned under the heading "Description." In the case of the monograph on the more readily volatile substance, Ether, p. 34, no statement to this effect is made, hence it is suggested that it should be deleted in this case and also in the monographs on Acetone, p. 10, Carbon Tetrachloride, p. 98 and Chloroform, p. 106.

The boiling point of Alcohol is required to be determined by Method I, p. 432, which defines the term "boiling point" as "that range of temperature within which at least 95 per cent, by volume, of the substance, distils." The monograph, p. 39, states that "alcohol boils at *about* 78° C.;" this statement, being extremely vague, leaves the analyst in doubt as to what range on each side of the figure 78° C. he can allow. It has been our experience that many samples of Alcohol, which meet all the requirements of the U. S. P., do not yield a distillate of 95 per cent by volume *at* 78° C.

It would be satisfactory if the U. S. P. gave a definite range for the boiling point, as in the case of Ethyl Chloride, p. 36 (between 12° and 13° C.).

Aldehyde or Oak Tannin Test.—In this test the phrase "at once" must be taken to mean what it literally implies, for the U. S. P. states on p. 2 that "In testing chemicals for innocuous impurities it is understood that five minutes shall be allowed for the reaction to be observed unless otherwise specified."

On conducting a series of tests with concentrations of acetaldehyde varying from 0.5% to 10%, we found that even a 10% concentration did not give a "yellow color" until after a period of 3 minutes, while, with a concentration of 3%, no tint was produced until 5 minutes had elapsed and 11 minutes was needed for the appearance of a distinct yellow color. From our series of tests, we found that, if a time of 30 minutes is allowed to elapse, a concentration of 1% can be detected, while 0.5% gives a positive reaction by the end of 50 minutes.

In the case of tannin, however, a concentration of 0.001% produces a faint yellow tint *at once*, the color deepening slightly on standing for 50 minutes; while a concentration of 0.0001% although giving no positive reaction *at once*, shows a faint yellow tint at the end of 50 minutes. This test then, as given in the U. S. P., will detect small quantities of tannin, but is unsatisfactory for aldehyde. It is suggested that aldehyde is best tested for by Murray's test, which is given below.

Test for Organic Impurities, Aldehyde, etc.—This test gives negative results with 1% Formaldehyde, 2% Acetaldehyde and 1% Acetone, but 1% Fusel Oil, 0.1% Furfural and 0.00001% Tannin are the minimum concentrations giving just more than the "faint brownish tint" that the U. S. P. allows.

Murray ("Standards and Tests for Reagent Chemicals") and Mallinckrodt ("Methods of Testing Reagent Quality Chemicals") use the following test for Aldehyde; "Mix 10 cc. of alcohol with 10 cc. of water, add 2 cc. of ammoniacal silver nitrate solution and allow to stand 12 to 18 hours in a dark place. No color or turbidity should develop." It is necessary, of course, for the ammoniacal silver nitrate solution to be freshly prepared. On carrying out a series of tests over a period of 18 hours, the smallest quantity of Acetaldehyde that we could detect by this means was 0.001%, which concentration produced a faint brownish tint.

With Murray's permanganate test for Organic Impurities, we were able to detect 0.5% Acetaldehyde, but not less than 3% Formaldehyde, 3% Fusel Oil and 0.07% Furfural.

Acetone Test.—This, inserted as a distinctive test for the presence of acetone, seems un-

suitable for this purpose since a violet or violet-red tint is produced by acetaldehyde as well as by acetone. Equal concentrations of these two substances produce almost identical colorations, and a concentration of 0.5% of either is the minimum quantity which can positively be detected. With a concentration of 1% or more, it is possible to distinguish between acetone and acetaldehyde by the addition of 5 cc. of ammonia T. S.; in the case of acetone, the color is almost completely discharged, while, with acetaldehyde, a yellow color appears. As the U. S. P. test is not specific for acetone, a better method for detecting it should be found.

Isopropyl Alcohol Test.—It has frequently been stated in the literature that this test is unsatisfactory, since pure isopropyl alcohol, under these conditions, produces a white, and not a yellow precipitate; it has been shown that a yellow precipitate is caused by the presence of impurities in the isopropyl alcohol. The appearance of a white or yellow precipitate, therefore, does not signify the presence of isopropyl alcohol, since various compounds produce such precipitates under the conditions of the test. The most recent work on this test is that of Matthes and Schutz (*Pharm. Ztg.*, 3 (1929), 44).

Benzaldehyde, p. 76.—The test for nitrobenzene in benzaldehyde, if carried out exactly as described in the U. S. P., is quite unsatisfactory; in the first place, if no nitrobenzene is present, no turbidity is produced on the addition of water to the alcoholic solution; secondly, using zinc and dilute sulphuric acid no evolution of hydrogen can be obtained, owing to the blanketing effect of the benzaldehyde on the zinc; hence it is impossible to finish the test.

If a color test for nitrobenzene is desirable, the following modification of the U. S. P. test can be used: "To 1 cc. of Benzaldehyde add 3 cc. of hydrochloric acid, and 0.5 Gm. of zinc dust and heat gently for 30 seconds; allow to stand for one minute, and dilute with 10 cc. of distilled water. Filter, and add 3 drops of potassium dichromate T. S.; no green color develops." The smallest amount detectable with certainty by this test is 2% of nitrobenzene; with concentrations of 2% to 5% the green color varies from an olive green to a deep bluish green, from 5% to 50% from a brownish-green to a dark brown; with a concentration of 10% a deep reddish purple color was obtained and this was the nearest approach to the "violet color" mentioned in the U. S. P.

The test for nitrobenzene, as described in the monograph on Oil of Bitter Almond, p. 249, was carried out on samples of benzaldehyde adulterated with nitrobenzene; this test slightly modified as follows, will detect a minimum of 2% of nitrobenzene: "Add 10 drops of Benzaldehyde to 5 cc. of alcohol in a 50 cc. flask; add 0.3 Gm. of zinc dust and 2 cc. of acetic acid and boil the mixture for 30 seconds; add sodium hydroxide T. S. until strongly alkaline, then 5 drops of chloroform, boil for 30 seconds and cool for 5 minutes; no odor of phenylisocyanide develops." This phenylisocyanide test is preferable to a color reaction since it is more definite and equally sensitive.

Chloral Hydrate, p. 104.—The formula for this substance is given as $CCl_3CHO.H_2O$. Since it does not behave as a typical aldehyde and is not considered to contain the —CHO group, the formula is generally written as $CCl_3CH(OH)_2$, and should be the one used in the U. S. P.

Under the heading "Tests for purity" the following test appears: "Gently ignite 2 Gm. of Chloral Hydrate: no inflammable vapors are evolved (difference from chloral alcoholate)." If this test is intended as a test for purity it is unsatisfactory in that no less than 15% of chloral alcoholate can be detected with certainty by this means. From the wording, however, "difference from chloral alcoholate," it would appear that this test is intended as a "Test for identity;" if this is the case, it would seem to be superfluous since these two substances, when pure, differ greatly in crystalline structure and are readily recognizable. If a test is needed, it is suggested that it should be worded as follows: "Gently ignite 2 Gm. of Chloral Hydrate: no inflammable vapors are evolved and no residue of carbon remains (difference from chloral alcoholate)" and inserted under the heading "Tests for identity." If it is necessary to test for the presence of small quantities of chloral alcoholate as an impurity, a new test must be devised.

Colchicum Corm, p. 115.—In the assay of this drug, the first filtration is difficult owing to the presence of mucilage formed from the starch present in the corms, and it is impossible to obtain 200 cc. of filtrate without resorting to the use of suction; mention of this fact should be made in the monograph.

Since, in this assay, the alkaloid is neither weighed nor titrated, but its proportion only evaluated by difference, it is suggested that the literature should be searched and, if possible, a

direct method substituted for the present assay, which, from our experience, is by no means satisfactory.

Glycerin, p. 180.—In this monograph, tests for oxalate and chloride are directed to be made on an aqueous solution of glycerin; that for chloride should be reworded as follows: "—or of 2 cc. of diluted nitric acid and 0.5 cc. of silver nitrate T. S. (chloride)." From a neutral solution of silver nitrate, as given in the U. S. P., oxalates are precipitated as well as chlorides; since oxalates are separately tested for with calcium chloride, the silver nitrate test should be made distinctive for chlorides.

Corrosive Mercuric Chloride, p. 187.—In the assay of this substance, the use of carbon tetrachloride for washing the precipitate free from adhering sulphur is extremely unsatisfactory, sulphur being soluble to the extent of less than 1% at ordinary temperatures. Carbon disulphide, in which sulphur is readily soluble, should be substituted.

Modified Dakin's Solution, p. 225.—From information received from various sources it appears doubtful whether any retail pharmacist in the City of New York ever makes this preparation. Attempts were made to purchase "Modified Dakin's Solution, U. S. P." from four of the largest wholesale druggists in the city; only one wholesaler could supply a sample; two others suggested the buying of a well-known proprietary article which is a stabilized hypochlorite solution.

The sample supplied by the wholesaler assayed only 0.303% of NaOCl (U. S. P. limits 0.45% to 0.50%), and showed an excess above the maximum alkalinity allowed by the U. S. P. tests for purity. From qualitative tests carried out, it would appear that this sample was not prepared by the U. S. P. method.

The proprietary article mentioned above assayed 0.997% NaOCl, being twice the U. S. P. strength; it also gave a red color in the "maximum alkalinity" test, showing that it was too strongly alkaline.

One of our largest manufacturers of surgical dressings markets the ingredients necessary for the extemporaneous preparation of a Dakin's solution which meets the Assay and Tests for Purity requirements of the U. S. P., though it is not made from the same initial chemicals; the ingredients supplied are a package containing a definite weight of sodium carbonate and a tube containing a definite quantity of liquid chlorine, which are to be added to a liter of water according to specified directions. This easily prepared solution assayed 0.482% NaOCl, and met the U. S. P. requirements for alkalinity.

Some method should be devised by which this important solution may be prepared more readily than is possible by the U. S. P. process.

Methenamine, p. 238.—In connection with the statement that "an aqueous solution of Methenamine is alkaline to litmus paper," no guidance as to the strength of the solution to be used is given. On examination of four manufacturers' samples it was found that, in using litmus paper sensitive to N/250 alkali, 2% solutions gave no reaction, while 10% solutions showed such a very faint alkalinity that the result must be said to be doubtful.

If a test for the alkalinity of methenamine is important, it could be stated similarly to that given under Smallpox Vaccine, p. 418. The following wording is suggested: "An aqueous solution of Methenamine (1 in 20) gives a red color with phenol red T. S. and is colorless with thymolphthalein (1% alcoholic solution)."

The p_H value of the samples examined was about 8.5.

Oil of Bitter Almond, p. 249.—It is recommended that the nitrobenzene test should be modified as described in this paper under Benzaldehyde. A concentration of 2% of nitrobenzene is detectable by this means. The color test for nitrobenzene previously mentioned may also be used, a similar range of colors with different concentrations being obtained.

Oils of Caraway and Cinnamon, pp. 253, 256.—There are upon the market, from reputable distillers, samples of these oils, labelled U. S. P., which cannot be assayed by the U. S. P. X process. In changing the method from that of the U. S. P. IX, while the same quantity of oil was employed, the size of the flask was reduced from one of 200 cc. to one of 100 cc. capacity, and sodium bisulphite was substituted for acetic acid for the purpose of neutralizing. It is impossible, in the smaller sized flask or even in a 200-cc. flask, to add sufficient sodium bisulphite to neutralize the mixture, consequently only very low and by no means concordant results, which cannot possibly be correct, can be obtained. If the method of the U. S. P. IX is used, satisfactory

assays, yielding consistent figures, can be carried out. As an example, a sample of Oil of Caraway labelled U. S. P., was assayed, with the following results:

	U. S. P. X Method.	*U. S. P. IX Method.*
1st Determination	27% Carvone	54% Carvone
2nd Determination	38% Carvone	55% Carvone

Similar results were obtained by these methods on samples of Oil of Cinnamon. Hence a return should be made to the method of the U. S. P. IX.

Phenol, p. 283.—When assaying samples of liquefied Phenol by the method given in this monograph, the stated quantity of 1 cc. of chloroform may not be sufficient to dissolve all of the tribromphenol present; if the amount of chloroform were increased to "2 cc. or a sufficient quantity to dissolve the precipitate," the assay would be entirely satisfactory.

Spirit of Ethyl Nitrite, p. 349.—In this monograph, the directions for the assay show discrepancies when compared with the general method for "Gasometric Estimations" given on pp. 437–439. Since reference on p. 349 is made to p. 437, it is desirable that the same method of procedure should be given in both places.

In the case of Spirit of Ethyl Nitrite, as well as of Amyl Nitrite, p. 49, 5 cc. of diluted sulphuric acid (10%) is directed to be used, whereas in the general method, p. 437, normal sulphuric acid (4.9%) is specified; which is the analyst to use?

The two monographs on pp. 50 and 349 state that corrections for temperature and pressure must be made in the calculation of the percentage of active constituent, when these vary from the U. S. P. standard of 25° C. and 760 mm. If these corrections are applied to the *"quotient,"* and if each correction is made separately and added or subtracted as necessary, as directed in the monographs, a different percentage is obtained from that which would result if the correction were applied to the *volume of gas* measured. On p. 438, *factors* are given for temperature and pressure corrections, hence the processes of addition and subtraction do not enter into the calculation, so it is immaterial whether the corrections are made on the volume of gas or on the percentage obtained, though for the sake of clarity and accuracy of wording the sentence "Correct this volume for temperature and pressure according to the following tables" should be inserted on line 7 of p. 438, between the words"-tube." and "Multiply."

On p. 438, the following passages occur:

"For pharmacopœial purposes, the determination will be sufficiently exact if the evolved gas is measured within 3° above or below 25° C."

"The barometric correction is important at any locality more than 250 meters above sea level."

Then follow tables giving Factors for Correction of Temperature and Barometric Pressure. It is inferred from these quotations that corrections for temperature are unnecessary between 22° C. and 28° C., and that small variations in pressure at altitudes below 250 meters are not "important," and therefore may be neglected. This interpretation is reasonable, since the percentage of active constituent in Spirit of Ethyl Nitrite may vary between 3.5% and 4.5% (a variation of about 25%), while temperature corrections between 22° (factor 1.010) and 28° (factor 0.990) only amount to 1% above or below the factor 1.000 for 25°; also, variations in pressure are unlikely to be more than 3% to 4% on either side of the factor 1.000 for 760 mm., unless the altitude is greater than 250 meters, since barometric pressure varies by about 25 mm. for a change of approximately 250 meters in altitude. It can readily be seen that small corrections such as these can only produce small changes in the percentage of active constituent, that is, changes in the second place of decimals. Such changes, however, when the results are close to the limiting figures of the U. S. P., may be great enough to cause the passing of a bad or the rejecting of a good sample.

Bearing these considerations in mind, the author suggests the following rewording for the monograph p. 349:

"—volume of gas collected; correct this volume for temperature and pressure, according to the Tables given on p. 438. Multiply this corrected volume in cc. by 0.307 and divide the product by one-tenth of the weight of the Spirit of Ethyl Nitrite taken; the quotient represents the percentage of ethyl nitrite in the liquid."

The subject of temperature and pressure corrections is again referred to in this paper under the heading "Gasometric Estimations."

Mercurial Ointments, pp. 413, 414.—The U. S. P. states that a colorless solution should result from the treatment of these ointments with nitric acid, when carrying out this assay; it is impossible to obtain this condition, a yellow color being always present. The required reaction with nitric acid is complete within ten minutes, and so the following rewording of this part of the assay is suggested: "warm the mixture gently for 10 minutes, when red fumes should no longer be evolved."

Gasometric Estimations, pp. 437–439.—Reference has already been made in this paper under the heading "Spirit of Ethyl Nitrite" to the corrections for temperature and pressure to be applied to the volume of gas measured in these estimations; the insertion of a sentence on line 7 of p. 438 has been suggested.

If, as stated previously, it is to be inferred from paragraphs 2 and 3 on p. 438 that the Pharmacopœia intends to neglect small variations in temperature and pressure, why should not paragraph 2 be worded as follows and paragraph 3 omitted? "No corrections are necessary for temperature and pressure if the evolved gas is measured within 3° above or below 25° C. and 10 mm. above or below 760 mm." Giving a definite range of barometric pressure for which correction need not be applied seems more satisfactory than stating that "the barometric correction is important at any locality more than 250 meters above sea level."

A 3° change in temperature and a 10-mm. change in pressure only affect the percentage result in the second place of decimals, but in order to obtain uniformity of results especially when the question of "borderline samples" arises, it seems more satisfactory to require corrections for temperature and pressure to be applied in *every* calculation, in which case paragraphs 2 and 3 on p. 438 should be omitted altogether.

As sodium nitrite is not estimated gasometrically, the name of this substance should be omitted from line 9, page 438, and its factors from p. 439.

Proximate Assays, pp. 452–454.—Under the monographs on Cinchona, Hydrastis, Ipecac and Nux Vomica, which four drugs are assayed by Type Process A, it would be more definite and easier to follow, if in each case, when reference is made to the paragraph "Extraction of the Drug" on p. 453, it were stated at which step the process is to be taken up. For example, in the case of Cinchona, Type Process A is to be proceeded with from the words "stopper tightly" on line 4; for Hydrastis and Ipecac, the process is used from the beginning "Place the —;" for Nux Vomica, a start should be made at the words "stopper securely" on line 2.

Lack of uniformity is found in references made in the monographs to the "specified solvent" mentioned in the paragraph "Shaking Out with Immiscible Solvent" on p. 454; this is exemplified in the following quotations:

Belladonna—using "chloroform as the immiscible solvent for extracting the alkaloid from the aqueous liquid."
Cinchona—"use chloroform for the final extraction."
Hydrastis—"use ether for the final extraction."
Hyoscyamus—using "chloroform for the final extraction of the alkaloids."
Ipecac—"use ether for the final extraction."
Nux Vomica—"using chloroform as the immiscible solvent in shaking out the alkaline liquid."
Stramonium—using "chloroform as the immiscible solvent for extracing the alkaloids from the aqueous liquid."

It would be less ambiguous if the paragraph on p. 454 were headed "Final Extraction with Immiscible Solvent," and the wording in all the monographs were brought into line with that used in the cases of Cinchona, Hydrastis and Ipecac.

When the alkaloid is to be estimated by titration, mention should be made of the strength of the standard acid to be used; a twentieth-normal solution seems suitable.

Some authorities have recommended that, in alkaloidal assays, the final ether or chloroformic solution, which has been in contact with ammonia during the shaking out, should be washed with a little water before evaporation; our experience has shown us that, when this washing is carried out, more uniform and satisfactory results have been obtained.

In Type Process B, the drug is to be mixed thoroughly with the solvent and ammonia in a small glass percolator, the outlet of which has been packed with cotton; maceration for one

hour followed by percolation is then directed; it is impossible to carry out the mixing thoroughly without displacing the cotton. This is obviated if the maceration for an hour with solvent and ammonia is carried out in a flask, in which thorough mixing is possible, and percolation then proceeded with as directed in the U. S. P., after transferring the mixture completely from the flask to the percolator. We have found that this modification improves the process of the U. S. P.

Caines and Evers ("Year Book of Pharmacy and Transactions of the British Pharmaceutical Conference," 1926, p. 384, and *Quarterly Journal of Pharmacy*, London, 1928, p. 326), in a comparison of methods of assay of Belladonna Leaves, suggest that the ether-chloroform mixture should be made in the proportion of 4 to 1 by volume instead of 3 to 1 as in the U. S. P.; they claim that less emulsification is caused when this change is made.

Volumetric Solutions, pp. 495–510.—Substances which are to be used as primary standards require definite specifications; these are given under the heading "Reagents," pp. 470–485.

In the preparation of Hydrochloric Acid, Normal, p. 498, "freshly standardized sodium carbonate" is directed for the standardization; in the case of Sulphuric Acid, Normal, p. 508, "reagent anhydrous sodium carbonate" is to be used. Although the wording under these two headings differs, it is assumed that reference in each case is to "Sodium Carbonate, Anhydrous" p. 483. The specification for this chemical would be better if some limit for the water content were given; for example, a sentence similar to that given under "Potassium Bitartrate" p. 480: "Heat 5 Gm. at 100° C. for thirty minutes: no loss of weight should result."

The U. S. P. IX gave specific details for the methods of standardization of all volumetric solutions; since in most cases these are omitted from the U. S. P. X, different analysts will follow methods from different books of reference, wherein small variations in procedure will occur. If a strict uniformity of results is desirable, would it not be advisable to include all details of methods as was done in the U. S. P. IX? This question is worthy of consideration.

The various series of tests and assays necessary for this paper were carried out with the assistance of Samuel S. Liberman and Marguerite C. Dimler, to whom I wish to express my sincere thanks.

COLUMBIA UNIVERSITY, COLLEGE OF PHARMACY,
DEPARTMENT OF CHEMISTRY.

AMERICAN DENTAL ASSOCIATION ORGANIZES COUNCIL OF DENTAL THERAPEUTICS.

At its recent annual meeting the American Dental Association provided for the organization of a Council of Dental Therapeutics. The organization will coöperate with members of the dental profession in protecting them and the public against fraud and acquaint them with objectionable advertising of proprietary dental remedies. The Association's bureau of chemistry will serve the Council in reaching their decisions. The organization hopes to promote a larger use of the preparations of the U. S. P. and N. F. and it is also contemplated to examine drugs and dental proprietaries for inclusion in an "accepted list." The preparations which receive favorable recognition may be marked "Accepted by the American Dental Association." The latter action is worthy of careful consideration; reference is made to the Government experience under the Food and Drugs Act with its related legend—viewpoints are as subject to change as individuals.

The Council of Dental Therapeutics is composed of Paul J. Hanzlik, Stanford University; Percy R. Howe, Harvard University; Milan A. Logan, Harvard University; Arno B. Luckhardt, University of Chicago; John A. Marshall, University of California; Victor C. Myers, Western Reserve University; John T. Norton, University of Chicago; Ura G. Rickert, University of Michigan; Harold S. Smith, Chicago; and the following ex-officio members: Editor C. N. Johnson, Journal of the American Dental Association; Secretary Harry B. Pinney, of the American Dental Association; Samuel M. Gordon, chemist for the American Dental Association.

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AROMATIC SULPHURIC ACID.

BY C. M. SMITH AND E. H. HAMILTON.*

The U. S. Pharmacopœia has for many years listed among its preparations "Aromatic sulphuric acid." For making it the tenth edition directs the gradual and cautious addition of 109 cc. of ordinary concentrated sulphuric acid to 700 cc. of alcohol, with subsequent cooling and addition of 50 cc. of tincture of ginger, 1 cc. of oil of cinnamon, and enough alcohol to bring the total volume to one liter. It is stated that the finished product contains free sulphuric acid and ethyl sulphuric acid together equivalent to not less than 19% and not more than 21% of sulphuric acid, H_2SO_4. No statement of the relative proportion of free and ethyl sulphuric acid to be expected is given in the Pharmacopœia and the method of assay described leads only to an estimation of the "total sulphuric acid."

The presence of free sulphuric acid to the extent of 10% or more would bring this product within the scope of the Federal Caustic Poison Act. Therefore, in the enforcement of this act, it was necessary to determine whether the preparation may contain as much as 10% of the free acid. A search of the literature revealed that considerable work had been done on this problem but the results of various investigators were not in agreement and none of them covered exactly the points in which we were interested.

Attfield[1] in 1869 examined certain samples of aromatic sulphuric acid at intervals during a period of two weeks, and says he found no ethyl sulphuric acid at any time, all the acid being free and amounting to about 19%. As will be shown later, this statement is contrary to the findings of other investigators, including the

* Food, Drug and Insecticide Administration, U. S. Department of Agriculture.

[1] Prof. Attfield, "Note on Aromatic Sulphuric Acid," *Pharm. J.*, 10 (1869), 471.

present writers. Clarke[1] in 1887 examined five samples of aromatic sulphuric acid, reporting from 13.9% to 19.4% free sulphuric acid but these figures were based on the mistaken assumption that direct titration of the product will give the content of free acid, and his results are undoubtedly high. Brown[2] in 1912 discovered that the results obtained according to the assay described in U. S. P. VIII were incorrect and proposed new methods of analysis which appeared to give satisfactory results for both free and combined acid. In 9 commercial samples he found from 6.12% to 13.45% free sulphuric acid and also noted that the proportion of free acid decreased with lapse of time. Brown's methods were criticized by Penniman *et al.*,[3] who also showed that the change in the assay adopted in the ninth revision of the U. S. P. left that method still far from serviceable. They proposed the so-called Maryland method, according to which various commercial samples were found to contain about 27½% total acid and about 11% free acid. In 1920, Kelly and Krantz[4] first proposed the method for total acid which was later adopted in the tenth or present edition of the U. S. P. They reported that they were unable to get anything but very low results by the Maryland method, and made no effort to determine the free acid.

Between 1920 and 1928 Dunnicliff and his coworkers,[5, 6, 7, 8, 9, 10] published a series of articles dealing with equilibrium between ethyl alcohol and sulphuric acid or various acid sulphates. They did not consider aromatic sulphuric acid itself, but some of their results have direct bearing on the subject since the ginger and cinnamon probably exercise very little effect on the chemical relationships. In one of their papers they describe their methods for complete analysis including a determination of uncombined alcohol. They adopted the U. S. P. X method for total acid, and arrived at a value for actual free acid by calculation from this and the apparent free acid shown by a direct titration of the product. Their results show that the proportion of free sulphuric acid in a mixture of alcohol and sulphuric acid depends on the relative amounts used, on temperature, and on the age of the mixture. Nearly all of the experiments of Dunnicliff and his fellow workers

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[1] E. W. Clarke, "Acid Strength of the Aromatic Sulphuric Acid in Use," *Pharm. Era* (March 1887), 69.

[2] L. A. Brown, "An Improved Method of Assay for Aromatic Sulphuric Acid," *Ind. & Eng. Chem.*, 4 (1912), 512.

[3] W. B. D. Penniman, *et al.*, "The Hydrolysis of Ethyl Sulphuric Acid and the Assay of Aromatic Sulphuric Acid," *Ind. & Eng. Chem.*, 8 (1916), 904.

[4] E. F. Kelly and J. C. Krantz, "Assay of Aromatic Sulphuric Acid," JOUR. A. PH. A., 9 (1920), 775.

[5] Butler and Dunnicliff, "The Action of Alcohol on the Sulphates of Sodium," *J. Chem. Soc.*, 117 (1920), 649–667.

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[7] Dunnicliff and Butler, "Ethyl Hydrogen Sulphate," *J. Chem. Soc.*, T119 (1921), 1384–1392.

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[9] Dunnicliff, Sikka and Hoon, "The System: Sodium Sulphate, Sulphuric Acid–Ethyl Alcohol," *J. Phys. Chem.*, 30 (1926), 1211.

[10] Dunnicliff, Aggarwal and Hoon, "The System: Ammonium Sulphate–Sulphuric Acid–Ethyl Alcohol," *Ibid.*, 32 (1928), 1697.

were made with 100% sulphuric acid and alcohol, whereas aromatic sulphuric acid is made from reagents, each of which contains approximately 5% water.

Since previous determinations of the free sulphuric acid in aromatic sulphuric acid were unsatisfactory and since the work of Dunnicliff *et al.* was not directly applicable to our problem the following experiments were carried out.

In the first series of experiments three mixtures were prepared in the laboratory from concentrated sulphuric acid and 95% ethyl alcohol and were designated A, B and C. "A" was mixed exactly as described in the U. S. P. X under "Aromatic Sulphuric Acid," except that the tincture of ginger and oil of cinnamon were replaced by additional alcohol. "B" and "C" were made from the same quantities of reagents, but in each case the whole quantity of the acid was initially mixed with only a portion of the alcohol, the remainder of the alcohol being added later. After the mixtures had been prepared, they were analyzed, and then each was divided into two portions. One portion of each (A_1, B_1, C_1) was kept on the work-table at room temperature (which averaged about 25° C.), while the other (A_2, B_2, C_2) was set on the back of a steam-bath where the temperature remained close to 37° C. All the solutions were analyzed at the end of 3-, 10- and 23-day intervals. Not only the free acid but the total acid as well was estimated each time in order to see whether the latter appeared to decrease as Brown supposed, a phenomenon which he ascribed to the production of very stable diethyl sulphate. The methods of analysis used were as follows:

1. The U. S. P. X method for total acid, consisting of evaporation of a portion of the sample to dryness with 30 cc. of normal sodium hydroxide solution and back titration of the excess alkali was supplemented by a direct titration to the methyl orange end-point of another portion of the sample. This gives the sum of the free sulphuric and ethyl sulphuric acids, and from it and the total acid figure the free acid may be calculated.

2. Brown's method, according to which the portion of sample upon which the direct titration described under (1) was made is heated to boiling, treated with 2 cc. of concentrated hydrochloric acid, and the sulphate ion precipitated with barium chloride solution. The precipitate corresponds directly to the free sulphuric acid, and from it and the titration figures the total acid is calculated.

3. A cold precipitation method, which was the same as (2) except that the barium chloride solution was added to an aliquot of the sample at room temperature without previous titration, and no hydrochloric acid was added to augment the natural acidity of the preparation. It was hoped that any tendency toward high results for free acid due to hydrolysis of ethyl sulphuric acid in hot solutions (Brown's method) might be avoided.

Methods (1) and (3) were applied in all cases, (2) in only some of them. The total data obtained are too voluminous to report here in full, so that a few generalizations will first be made.

The results obtained for total acid are shown in Table I. No apparent decrease in total acid with lapse of time as reported by Brown and interpreted by him to indicate the formation of diethyl sulphate was evident. Therefore, all values obtained on both subdivisions of each preparation are reported as replicate determinations.

TABLE I.—"TOTAL SULPHURIC ACID" IN MIXTURES OF SULPHURIC ACID AND ALCOHOL.

Sample.	A.			B.			C.		
Method.	1.	2.	3.	1.	2.	3.	1.	2.	3.
Range, %	19.46 to 20.03			19.60 to 20.03			19.30 to 19.88		
		19.28 to 19.73			19.57 to 19.73			19.49 to 19.69	
			19.60 to 20.40			19.79 to 20.22			19.65 to 20.19
Average, %	19.72			19.78			19.69		
		19.54			19.64			19.60	
			19.97			20.01			19.93

All the methods show that A, B and C are practically identical, as they should be since they were made from the same quantity of reagents. Method (2) gave uniformly lower results and method (3) uniformly higher ones than the U. S. P. method, but the differences are barely significant. Method (2) (Brown's) gave the most reproducible results, the standard deviation for it being about one-half what it was for the other two methods. The Maryland method was not tried.

Considering that there was so little difference in the methods used we selected (1) as the basis for further work, mainly because it represented practically the average of all three methods and is sanctioned by the U. S. P.

In Table II are given the results for free sulphuric acid, obtained by method (1). Because of the rather poor reproducibility of the method, the results have been rounded off to one decimal place. All samples were also analyzed by method (3) and some by method (2). The results by (2) averaged 0.15% above, and those by (3) 0.25% below the reported figures.

TABLE II.—FREE SULPHURIC ACID IN MIXTURES OF SULPHURIC ACID AND ALCOHOL.

		A_1.	A_2.	B_1.	B_2.	C_1.	C_2.
Specific gravity			0.945		0.945		0.945
Total H_2SO_4			19.7%		19.8%		19.7%
Free H_2SO_4	*On day prepared*		16.6%		11.8%		9.2%
	After 3 days	14.1%	9.9%	10.1%	7.6%	8.6%	7.0%
	After 10 days	10.7%	5.3%	8.3%	5.2%	7.4%	5.1%
	After 23 days	7.8%	5.3%	6.6%	5.2%	6.2%	5.2%

The results in Table II show that even immediately after preparation, the free acid is less than the total, indicating the formation of ethyl sulphuric acid during mixing. The quantity present is dependent upon the proportion of alcohol and acid used in the initial mixing, but in the opposite sense to what might be expected from Dunnicliff's experiments. This fact is probably explained by the different temperatures which the different mixtures attain. The mixtures which contained the lesser proportions of alcohol attained the higher temperatures during mixing and a high temperature evidently accelerates the formation of ethyl sulphuric acid.

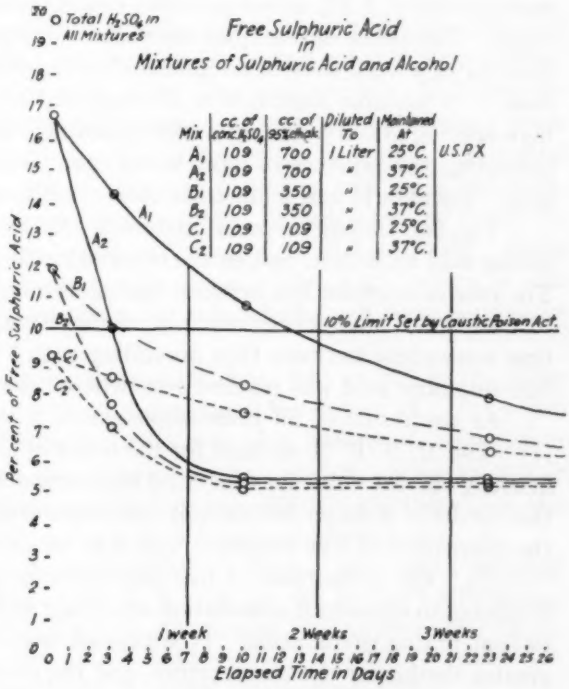
Next it is seen that the free acid does not remain constant, but decreases in all cases and at a faster rate in those preparations kept at the higher temperature. The warmer samples reached a fixed equilibrium value sometime between 3 and

10 days, and the cooler samples were evidently tending toward about the same values. That all samples should approach approximately the same equilibrium value is consistent with the fact that they all contained the same proportion of reagents.

In all the samples except one (A_1) the free acid had decreased to 10% or less in 3 days. The one exception, which was the sample prepared according to the directions of the U. S. P. X and kept at ordinary room temperature, passed the 10% mark somewhere between 2 and 3 weeks.

The equilibrium value for free sulphuric acid indicated by Dunnicliff's work for a product containing 20% total acid is approximately 3%. The higher value, about 5.2%, indicated by our work, is no doubt due to the fact that our mixtures contained about 5% water, which was not present in Dunnicliff's preparations.

The following set of curves present in graphical form the data of Table II. The trend of all the curves toward a common value is very evident.


Free Sulphuric Acid
in
Mixtures of Sulphuric Acid and Alcohol
O Total H_2SO_4 in All Mixtures
Mix | cc. of conc. H_2SO_4 | cc. of 95% alcohol | Diluted To | Maintained At
A_1 109 700 1 Liter 25°C. U.S.P.X
A_2 109 700 " 37°C.
B_1 109 350 " 25°C.
B_2 109 350 " 37°C.
C_1 109 109 " 25°C.
C_2 109 109 " 37°C.
10% Limit Set by Caustic Poison Act.
Per cent of Free Sulphuric Acid
1 week
2 Weeks
3 Weeks
Elapsed Time in Days

In order to confirm these results as applying to aromatic sulphuric acid itself, 8 samples of this product were purchased in the open market, labeled D to K inclusive, and analyzed. Three of these, I, J and K, were the products of large manufacturing firms, and their ages were consequently unknown. The other five were obtained from retail druggists, by whom they had been prepared. Of these five, three, D, E and F, were obtained from Dr. S. L. Hilton, treasurer of the Board of the United States Pharmacopœial Convention, who kindly furnished us with the dates on which two were prepared and personally prepared the third on the day of purchase. Of the remaining two retail products, one, H, was at least a year old, the other, G, freshly prepared on the day of purchase.

Method of analysis (1) was used for reasons already stated. The brown color of the tincture of ginger rendered the methyl orange end-point in the two titrations somewhat less definite than in the previous set of experiments, so that the results are perhaps not quite so accurate as before. A control experiment with tincture of ginger and oil of cinnamon alone showed that they were so nearly neutral that no correction had to be made for them. The results obtained are given in Table III.

It may be seen that the specific gravities of the samples are nearly all equal to or higher than the value of "about 0.94" quoted by the U. S. P. X. Farther, in

TABLE III.—ANALYSES OF COMMERCIAL AROMATIC SULPHURIC ACIDS.

	D.	E.	F.	G.	H.	I.	J.	K.
Date made	7/3/19	9/21/25	5/27/29	5/27/29	Unknown but old	Unknown	Unknown	Unknown
Sp. gr.	0.940	0.940	0.942	0.934	0.959	0.951	0.954	0.947
Total H_2SO_4	19.8%	19.7%	20.1%	18.5%	20.3%	20.5%	21.6%	20.0%
Free Sulphuric acid 5/28/29	5.2%	5.3%	15.9%	16.5%	7.6%	6.2%	5.3%	5.7%
Free Sulphuric acid 6/4/29			10.1%	11.3%	7.7%	6.3%		
Free Sulphuric acid 6/18/29			6.5%	7.5%				

six cases the total acid is within the U. S. P. limits, and in the other two not far removed from them. Several interesting points are evident in connection with the figures for free sulphuric acid. Three of the old samples contained practically the same quantity, 5.2% as our previous experiments had shown to be the equilibrium value. The other old samples showed more than this, and yet a reëxamination of them after a week showed no further change, showing that they too were at equilibrium. A possible explanation is suggested by the fact that these samples had high specific gravity without a correspondingly high content of total sulphuric acid, indicating the presence of more water than usual; a condition causing higher free acid. Samples H and I illustrate these conditions.

The two freshly prepared materials "F" and "G" show a decrease in free sulphuric acid with time, just as was observed with the samples made in the laboratory. The rate of decrease lies between that shown by "A_1" and "A_2," probably because "F" and "G," having been made in warmer weather, were maintained at a temperature somewhere between that prevailing with "A_1" and "A_2." A content of 10% free sulphuric acid was reached somewhere between one and two weeks.

As the result of all these experiments it may reasonably be concluded that (1) The U. S. P. X method for the assay of aromatic sulphuric acid gives a sufficiently correct value for the "total sulphuric acid" present. From this value and the results of a direct titration of the preparation to the methyl orange end-point the proportion of free sulphuric acid may be calculated.

(2) The proportion of free acid initially present is about 16% H_2SO_4, but is subject to considerable variation according to how much the product is permitted to heat during preparation. It decreases with time, the rate of decrease being greater the higher the temperature, and the product, if kept at 25° C., approached an equilibrium limit of about $5^1/_4$% H_2SO_4. Thus while the preparation contains more than 10% free sulphuric acid initially, it will contain less than 10% after standing. Usually two weeks are sufficient.

THERMOMETER MANUFACTURERS.

Congressman Bloom, who sponsored a proposal to have all clinical thermometers tested and certified by the United States Bureau of Standards, has announced that this would entail too much work and difficulty and that the problem of securing only high-grade, accurate instruments can best be solved by permitting their manufacture only by firms licensed to uphold a high scientific standard.

CHAIN STORE INQUIRY.

State of Minnesota:
St. Paul, February 1st.

An investigation of nine groups of chain stores in the City of Minneapolis by the attorney general is sought in a complaint filed by the owner of a grocery store in that city, who alleges that the chain stores are being operated in violation of the Sherman Anti-Trust Act and of the Minnesota statutes.

FLUECKIGERIANA.*

BY EDWARD KREMERS.

IV. LLOYD'S CONFERENCE WITH FLUECKIGER IN NEW YORK.†

As stated in a note on letters written by Professor Flueckiger to Dr. Frederick Hoffmann, 1891 to 1894,[1] the Strassburg professor after his retirement from the then Kaiser Wilhelm's Universitaet had intended to devote the remaining years of his life to a history of the "Drogenkunde." Preliminary work toward this end soon made him realize that an important, if not a large, part of the information sought had to be gained in America. It was for this reason that he at last accepted the oft-repeated invitation of his friend, Dr. E. R. Squibb, to come to this country as his guest. Such he became during the months of June, July, August and September of 1894.[2]

Once in this country it was inevitable that he should want to see the historical material on American materia medica collected by Lloyd and, what was even more, have a conference with the collector who, more than any one else, had thus far contributed toward a *Pharmacographia Americana*.[3] Flueckiger's advanced years and consequent indisposition, aggravated by an extremely hot spell, prevented the drug historian of Bern from undertaking the fatiguing trip to Cincinnati. Professor Lloyd then did the next best thing possible: he sent cases of books to Squibb's laboratory where Flueckiger could look them over at his leisure. More than that, at the invitation of Dr. Hoffmann he came to New York[4] where he and Professor Flueckiger met to talk over the subject in which both were so greatly interested.

Unfortunately, Professor Flueckiger's untimely death put an end to the plans formulated by the father of modern pharmacognosy and the author of "Drugs and Medicines of North America." Unfortunate as was this failure of coöperation in the history of drugs, the attempt should be properly recorded. Since no better record exists than a letter by Professor Lloyd, it is, herewith, published for the benefit of future students of American drugs and American pharmacy.

Inasmuch as the original study was undertaken for the purpose of securing contributions to a chapter in the life of Dr. E. R. Squibb, the letters by Professor Lloyd contain references to Dr. Squibb which are likewise of interest to the future

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* Section on Historical Pharmacy, A. PH. A., Rapid City meeting, 1929.

† Nos. I, II and III have previously been published in the *N. Y. Apotheker Zeitung:* I. Briefe Flueckiger's an Hoffmann, 45 (1924), 110, 122. II. Aus dem Tagebuch Augusta Flueckiger's, 49 (1928), 57. III. Flueckiger's Amerika Briefe an Tschirch, 49 (1929), 142, 155; also, 50 (1929), 1 and 15.

[1] *N. Y. Apoth. Ztg.*, 45 (1924), 110.

[2] *Ibid.*, 49, 57; see also Flueckiger's American letters to Tschirch, do. 49, pages 142 and 155; also do. 50, 1 and 15.

[3] Unfortunately the correspondence between Flueckiger and Lloyd has not been preserved, at least no letters have been found thus far either in Strassburg or Cincinnati, though a careful search for them has been made at the writer's request.

[4] Under date of June 27th, Professor Flueckiger's daughter recorded in her diary that they had dined with Dr. and Mrs. Hoffmann at 112th St. and that at their home they had met Professor Lloyd. This note, therefore, establishes the exact date of Professor Lloyd's visit with Professor Flueckiger.

biographer of this early pharmaceutical manufacturer and consequently to the historian of American pharmacy.

Herewith follows the greater part of a letter written by Lloyd under date of December 22, 1922:

> "In the year 1894 I received a letter from Dr. Fred. Hoffmann, stating that Professor Flueckiger was arranging to visit America and hoped to be able to make the trip to Cincinnati and spend some time in the Lloyd Library. I replied to the effect that it would please me, could the arrangement be made, and in accordance therewith the plan was to have him spend as much time as he could spare with me.
>
> "On his arrival in New York he became the guest of Dr. Edward R. Squibb of Brooklyn, making his home his headquarters during his New York stay. Unfortunately, one of the most severe heat spells we have ever known in America struck our country soon after his arrival. Dr. Flueckiger was not strong. To him the journey to Cincinnati seemed a mighty task and reluctantly he was forced to abandon it.
>
> "Then he wrote[3] to me stating his real object in visiting Cincinnati, which was to study *Americana* as found in the Lloyd Library and to converse with me regarding the problems of America's materia medica and medicinal plants. He asked me if I could not forward to him in Brooklyn books that bore on this subject in order that he might in a cursory manner consider the subject as a whole.
>
> "I packed up for him several large boxes containing several hundred volumes bearing on the early record of the American materia medica and medicinal plants, sending them by express to him in care of Dr. Squibb at his home.
>
> "Within a very short time, I got a letter of invitation from Dr. Hoffmann, asking me to come to New York, meet Dr. Flueckiger and talk over the subjects he had in mind. Dr. Hoffmann invited me to make my stay in New York at his home, which invitation I very gladly accepted, starting immediately for New York.[4]
>
> "In the visits (I do not know just how many I had) the meetings with Dr. Flueckiger were at Dr. Hoffmann's home or at the office of the *Rundschau*, which he then edited. Subjects of interest and importance were talked over, and at the suggestion, I might even say request of Dr. Flueckiger who expressed his inability to accomplish the work he had designed unless I coöperated with him, an arrangement was made by which the American drugs and medicines were to be presented in a manner similar to that of the 'Pharmacographia,' and which when prepared would be published under the name of Flueckiger and Lloyd instead of Flueckiger and Hanbury as was the 'Pharmacographia.' This was a very great honor to me, a mighty surprise, but notwithstanding my timidity in accepting such a responsibility, under the advice of Dr. Hoffmann I did so.
>
> "The arrangement was to the effect that I should write the historical record of the drugs used in American medicine and those introduced and established, especially by the Eclectic School of Medicine, with which school Dr. Flueckiger seemed, to my surprise, to be well acquainted.

"The heat wave, however, struck New York as well as the Middle West, and Dr. Flueckiger, if I remember correctly, cut his visit short, embarking very soon after my trip to New York for his home.[1]

"Immediately I started to work on the subject we had in mind. Before anything material had been accomplished, Professor Flueckiger died, thus putting an end to the arrangement, much to my disappointment.

"Into the hands of Professor Schaer who followed Flueckiger in the University came the documents that had passed between us, and Professor Schaer published in Germany at least two of the articles from my pen. They were titled—'The California Manna'[2] and 'The Destruction of Tobacco in Virginia by Act of General Assembly, January 6, 1639, under Sir Francis Wyatt, Governor.'[3] Of these I have a reprint of 'The California Manna'[4] and Miss Wycoff has made for you a copy of the other, both of which are enclosed herewith."

The occasion of Flueckiger's visit caused the *Pharmaceutical Era* to direct attention to the Lloyd collection at Cincinnati under the caption "A valuable and unique library." (Oct. 1894.)

That Lloyd had been coöperating with Flueckiger even before this, has already become apparent from a statement made by the latter in a letter to Hoffmann dated December 1, 1891.

Although the correspondence has been lost, as previously stated, Professor Lloyd kindly supplied additional information in a letter dated January 17, 1924, from which the following paragraphs may be quoted:

"I remember well the incidents connected therewith, one being a desire of Flueckiger to study the Hydrastis problem directly from a plant grown by himself, the other being the study of Senega concerning which I had written several articles and in which I endeavored to discreetly controvert the opinion Professor Maisch had taken to the effect that *Polygala Boykinnii* was the false Senega that had recently entered commerce. The only specimen of *Polygala Boykinnii* that Professor Maisch had at his command or that he had received was a single specimen that had come to him from the South, whereas the "Spurious Senega" or "Large Senega" that entered commerce came from Minnesota, mainly supplied by a drug grinding firm who united with me in establishing the fact I have mentioned. Professor Maisch did not take kindly to this correction that was made in a very genteel manner, as I thought, and attempted to controvert the same in an article published in the *American Journal of Pharmacy*, to which article I did not reply because the facts were all on my side and need not be discussed. This controversy to-

[1] From both the diary of Miss Flueckiger and Flueckiger's American letters to Tschirch, it becomes apparent that Lloyd confounded the excursions which the Flueckiger family took with their host, Dr. Squibb, to cooler regions with his return to Europe much later.

[2] As stated by Prof. Lloyd, the first of these contributions was published in Germany, *viz.* in the *Ber. deut. Pharm. Ges.*, 7, page 245. (Reported June 3, 1897.) The English reprint to which he refers was one from the *Am. Jour. Pharm.*, 69 (July 1897).

[3] This copy has been filed with Professor Lloyd's letter.

[4] Comp. *N. Y. Apoth. Ztg.*, 45 (1924), 110.

gether with the description of Senega known in commerce as "Large Senega" interested Flueckiger very much and hence his request for Senega.

"In connection therewith I will state I sent him Senega from every section of America, beginning in the East where Senega was first introduced, thence following throughout America the trend of its commercial progress, ending with the large Senega of Wisconsin and Minnesota, supplied by Mr. Huber,[1] the owner of the drug grinding establishment mentioned. I did not send him a specimen of *Polygala Boykinnii* for the reason that I could not obtain one.

"In my opinion you will find this entire Senega problem thrashed out to your satisfaction in the PROCEEDINGS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION and the *American Journal of Pharmacy* at about the period mentioned."

PRESCRIPTION BOTTLES.*

BY WILLIAM J. HUSA.**

The great convenience of washed and corked prescription bottles packed with corrugated cardboard, as compared with the unwashed, uncorked bottles packed in straw, as was the case a quarter of a century ago, might lead one to believe that this problem has been completely solved. It might appear that at the prescription counter no attention need be paid to prescription bottles except to make an occasional notation on the order book.

However, in spite of the careful control that is presumed to go along with large scale production, it will pay the pharmacist to carefully scrutinize the prescription bottles used in his store. In the first place, the bottles are not always clean enough for use; sometimes there is a smoky film and sometimes the bottles appear as though there is mold on the inside, due probably to the crystallization of mineral salts. Difficulties due to alkalinity, such as the precipitation of alkaloids from solutions of alkaloidal salts, etc., are still found all too frequently. In many cases the precipitation or other change occurs after the prescription has left the store and the pharmacist may not be aware of it. In some cases the trouble is prevented by merely washing the bottle before use; from this it would appear that the glass does not develop alkalinity in presence of water at ordinary temperature, but that the alkali in the bottle is probably formed by hydrolysis of the silicates composing the glass at elevated temperatures in presence of steam while the bottles are being dried subsequent to washing. An easy test for this alkalinity is to fill two or three bottles from each case with hot water to which a few drops of phenolphthalein T. S. has been added; if a coloration does not appear the bottle is satisfactory for use. My experience has been that the manufacturers are always willing to replace such defective bottles. The pharmacist should safeguard his patrons and the reputation of his store by proper attention to the quality of the prescription bottles used.

There are other points in connection with prescription bottles which might prof-

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[1] The Mr. Huber mentioned was, no doubt, Mr. J. C. Huber, senior member of Huber and Fuhrmann, drug sellers, Fond du Lac., Wisc.

* Section on Practical Pharmacy and Dispensing, A. PH. A., Rapid City meeting, 1929.

** Professor of Pharmacy, University of Florida.

itably be discussed, such as the use of round or square bottles for prescriptions intended for external use, and the questionable practice of many pharmacists of using the graduations on the bottles in compounding prescriptions, instead of utilizing graduates of a proper degree of accuracy. However, I will pass by these points at this time, in order to lay emphasis on another point, *i. e.*, the desirability of having available prescription bottles of amber-colored glass, in order to properly protect the contents from the deleterious effects of light waves.

The United States Pharmacopœia directs that many drugs and preparations should be stored in amber-colored bottles. Since these same substances are frequently kept for long periods of time by the ultimate consumer, it would be in accordance with the spirit of the pharmacopœia to insist that these be dispensed in amber-colored bottles.

In these days, when so much emphasis is being placed on the commercial side of pharmacy, it is not surprising to find glaring examples of neglect of the fundamental principles of dispensing. For example, let us consider the solutions of mild and strong silver-protein, which the Pharmacopœia directs should be freshly prepared and dispensed in amber-colored bottles. I ran across one store, in which *stock solutions* of these silver preparations were kept at the prescription counter. Only slightly less objectionable is the practice of dispensing pint or quart bottles of these solutions to physicians for office use, in cases where such a supply is sufficient to last for several months. Frequently these solutions are dispensed in ordinary bottles instead of in amber-colored bottles as directed by the United States Pharmacopœia. Another error made by pharmacists is the failure to advise customers that these particular solutions should be discarded after they are several weeks old.

While such errors in dispensing may be ascribed in part to lack of knowledge of the contents of the pharmacopœia and to thoughtlessness on the part of the pharmacist, part of the trouble is due to the fact that amber-colored prescription bottles of the usual style are not available. Recently, I had some correspondence with the vice-president of one of the large glass companies, in which I called attention to the desirability of having prescription bottles of amber-colored glass. It was made clear that the glass manufacturers could readily manufacture such bottles if there were a demand for them, but that they did not propose to create the demand.

Inquiries sent to some of the glass companies and associations brought the reply that prescription bottles of colored glass were not being manufactured. However, I have a prescription bottle of green glass which was used as a container for medicine purchased at a drug store several years ago by a member of my family. On investigation, I found that these bottles of dark green glass were sold to the pharmacist in quantity lots, the name of the drug store being stamped on the back of the bottle. If it is practical to use green bottles, which offer no protection from light, it would be more practical to use amber-colored bottles, which are known to decrease the rate of deterioration of materials sensitive to light.

It would seem that bottles of colored glass are readily available for soft drinks and other cheap materials, while expensive drugs which really need protection are allowed to go out in colorless bottles. It will be a credit to pharmacy and to this Section, if we initiate a movement here, through our Committee on Glass Standardization, or otherwise, that will ultimately make available to every pharmacist a supply of amber-colored prescription bottles.

DEPARTMENT OF BUSINESS MANAGEMENT

Conducted by Paul C. Olsen.*

COMMENTS, QUESTIONS AND SUGGESTIONS ARE INVITED AND WELCOME.

Readers are invited to submit comments, criticisms and suggestions regarding the material which appears in this department. The Editor also will undertake to answer questions regarding general problems of business management. Letters of general interest will be published, but the writer's name will not be revealed without his permission.

THE CHANGING EMPHASIS IN THE STUDY OF DISTRIBUTION COSTS.

BY PAUL C. OLSEN.

In 1922 a joint committee of the United States Senate and House of Representatives, officially titled the United States Congress Joint Commission of Agricultural Inquiry, made a monumental report. Overcoming difficulties which in the beginning seemed insuperable, the Commission collected facts which permitted the calculation of distribution costs for many important agricultural commodities. In addition, it calculated the share of these costs which were incurred by the producers themselves, the various wholesale distributors involved and the retail outlets through which these commodities finally reached the consumer.

When these studies revealed that one-half to two-thirds the price the ultimate consumer paid for important products of the farm and orchard was a payment for distribution costs, the popular opinion of the extortionate and unconscionable profits of the "middleman" seemed to be confirmed. Popular opinion always has inclined to the idea that when a retailer buys an article for sixty cents and sells it for a dollar, he has made forty cents clear profit.

Incidentally, it is betraying no secret to say that there were and are thousands of retail and wholesale distributors who hold the same opinion. What kind Santa Claus or other good fairy pays the rent and other costs incident to the conduct of these wholesale and retail businesses, I am unable to say.

One great value of this report of the Congressional Joint Committee, therefore, was its revelation to consumers and distributors alike that the tremendous spread between the price producers received for agricultural products and the prices ultimately paid by consumers was not caused by extortionate profits obtained by wholesale and retail distributors, but rather by the costs of admittedly necessary distributive activities. Freight, for instance, and the costs of refrigeration and storage. In fact, this Congressional survey revealed that the total of all the profits obtained by wholesale and retail distributors was so small that their entire elimination would have little or no effect on the price paid by the ultimate consumer. (Admittedly there are wastes and inefficiencies in the distribution of almost any product, but competitive conditions in distribution are such as not to permit, for long, extraordinary and unusual profits. In fact, competitive conditions tend even to enforce a considerable degree of distributive efficiency in order to permit any profits at all.)

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This Congressional investigation in 1922 was not the first wide-spread effort to get the facts on distributive costs. As far back as 1913, the Harvard University Bureau of Business Research undertook to collect these figures in so far as they applied to retail shoe stores. The first difficulty met was that an amazingly large number of shoe retailers kept no books at all or kept them in such a careless or illogical way that their records were of little or no value. A real contribution was made, therefore, when the Bureau devised an up-to-date and easily used system of operating accounts designed especially for retail shoe stores. It was not until 1919, however, that a sufficient number of shoe retailers had adopted this simplified accounting plan to permit a report to be made on their distribution costs. This is an illustration of the difficulties and delays incident to the progress of such a pioneer movement.

Results, however, were obtained more quickly with retail grocers. A report was issued early in 1915 of the typical or usual costs incurred by retail grocers during 1914. Since its pioneer efforts, the Harvard University Bureau of Business Research has published similar reports on the usual distributive costs incurred by manufacturers, wholesalers and retailers in seventeen different lines of business.

In addition, similar investigations have been made in these and other lines by other university bureaus of business research, trade associations and independent research organizations.

The value of all these studies is that they create a standard based on actual facts to which an individual operator can compare his own results. Before facts of this kind were collected and published, a shoe retailer, for instance, with wages of his sales force amounting to 14 per cent of sales had no idea whether or not this was a good or a poor showing. If the usual result reported by a hundred or more stores operating under conditions like his is 11 per cent, this certainly is evidence enough to warrant a serious inquiry as to why his costs for this particular item should be more than 25 per cent greater than the average amount paid by others facing similar conditions.

This is, of course, but one illustration of many which might be cited of the practical value of the creation of a standard to which an individual can compare his own distribution costs. There are, in addition, many other values which can be attributed to the collection of these facts.

One of the most important of these is the increased appreciation on the part of progressive business men—particularly retailers—of the necessity of accurate and up-to-date records. (Typical costs in a particular line of business are of no practical value to the individuals in it unless they have records of their own with which to compare the averages.)

Thus the old idea that an article bought for sixty cents and sold for a dollar produced forty cents clear profit has been gradually disappearing. Stated in accounting terms, there has come in recent years an increasing understanding and appreciation of the difference between gross and net profit.

One result of this growing understanding of the costs of doing business has been a demand upon manufacturers by wholesalers and retailers for discounts commensurate with the average costs shown by these recently revealed facts. For instance, retail druggists have argued that with costs in their stores averaging

28 per cent of sales, it is manifestly impossible for them to make even a small profit with a discount of less than $33^1/_3$ per cent of sales. In almost every line, manufacturers have been quick to accept this line of reasoning; consequently, in recent years, there have been marked upward tendencies in the discounts allowed wholesalers and retailers, particularly on standard merchandise.

Theoretically, the idea is sound. If a distributor obtains a gross margin on each and every item he carries which is larger than his average cost of doing business, his whole business is bound to be profitable because each and every sale is made at a profit. An obvious corollary to this hypothesis is that the larger the gross margin the greater the net profit from the sale of a particular item.

This is a beautifully constructed theory, but along came a group of shrewd merchandisers to upset it. The short line jobber is a familiar figure in groceries, drugs, hardware and tobacco. Coöperative buying associations owned by retailers are another type of wholesale outlet which follow the same policy. They sell a comparatively small number of the largest and fastest selling items at very low prices. For instance, a common practice of the short line jobber or the coöperative association in the drug trade is to rebate to retailers 10 per cent of the $16^2/_3$ per cent discount which is customarily received from manufacturers.

Average costs of doing business in the old line wholesale drug houses run from 15 to 16 per cent of sales. The wholesaler schooled in this theory immediately makes two claims. One is that he cannot afford to give away 10 per cent of his $16^2/_3$ per cent gross margin because his costs of doing business are 15 to 16 per cent of sales. The second is that those houses which do will soon find themselves in the sheriff's hands.

As everyone knows, these predictions of the early demise of the short line jobber, coöperative wholesaler and other cut price distributors have been vain. In fact, some of the conservative old line houses have had to follow the same policy in self-defense, but not without considerable misgivings. Strangely enough, they, too, are still doing business and in many cases making more money than ever. But more of that later.

In retailing, a similar situation has been precipitated by shrewd and far-sighted merchants. The cut price policies of the chain stores, mail order houses and department stores are the most familiar examples.

"How do they do it," inquires the anxious retailer. "My costs are 25 per cent of sales. How can I meet their prices when they are selling merchandise on a gross margin of 20 per cent?" Again come the familiar predictions of bankruptcy for the cut price merchants. Year after year, however, the price cutters go serenely on with amazing success.

The explanations were that the cut price items are merely loss leaders. With increasing price consciousness on the part of consumers and an enormous proportion of their business in the so-called cut price items, it appears as if the price cutters soon would be forced out of business if these items really are sold at a loss. What are the facts to support this assertion?

When our anxious retailer friend says his operating costs are 25 per cent of sales, he means that at the end of a year's business the total of all the expenses paid out during the year amounted to just 25 per cent of the total amount of the sales he made during the year. That is to say, the average cost of doing business

was 25 per cent of sales. Quite obviously, some sales were made, perhaps, at a cost much less than 25 per cent while others, unfortunately, were made at costs much greater than 25 per cent. All this merchant knows is that the average of all of them is 25 per cent.

If he knew the costs of carrying and selling individual items of merchandise in his stock instead of merely the average cost for all of them, he would gain two important advantages. Since it is a physical impossibility for him to give equal attention to all the items in his stock, he would know, then, definitely, the items in his stock which are sold most profitably and therefore the items on which he could concentrate selling effort most profitably.

Second, on items in which price competition proved to be keen, he would know definitely the extent to which he could reduce prices and still sell them at prices which, at least, did not produce a loss.

In the course of an investigation of the costs of carrying and selling individual items of merchandise, I had the good fortune to discuss these propositions with Dr. Paul H. Nystrom of Columbia University. Dr. Nystrom recounted the philosophy of a boyhood employer of his who conducted a general store in the middle west.

This merchant evidently was wise beyond his time. Canned vegetables in those days, as they do to-day, carry larger gross margins than most grocery store products. On the other hand, sugar is handled on perhaps the narrowest margin of all grocery store merchandise. While this merchant's competitors fought with each other to capture the canned goods trade of the community, he concentrated upon its sugar business. He wisely saw that gross margins and even net profits per unit sale are not the only determinants of the total net profits earned in a business. The volume of business done or possible to do in an item and the rate of turnover are also vital determinants of total net profits.

For instance, few vegetable hucksters grow rich even though the gross and net margins of profit are high and daily turnovers of merchandise stock are obtained; the volume of business that an individual huckster can do is too small. Similarly, a drug store with an annual volume of $2,000,000 would be considered an unusually large store. If, however, it had to maintain a stock of merchandise valued at $1,500,000 in order to do this business, the store would not be considered a successful one even if it earned a net profit amounting to 8 per cent of sales. The return on the investment in merchandise would be unattractive.

Recent investigations by the United States Department of Commerce and other responsible agencies definitely confirm the shrewd intuitive judgments of the far-sighted middle western storekeeper whose ideas I have quoted. An investigation in a wholesale grocery house showed distribution costs for different classes of commodities varying from 6 to 16 per cent of sales although the average for the entire house was 10 per cent. In the distribution of hardware and of paint and varnish, similar facts have been brought to light.

The National Wholesale Druggists' Association has found astonishing variations in costs and profits in different lines. In the retail drug trade, the Druggists' Research Bureau examined more than 177,000 individual retail sales. It found stores in which 2 per cent of the merchandise stock on hand accounted for 8 per cent of the sales and 16 per cent of the total net profits.

It is interesting and profitable to a business man to know that these variations in distribution costs for individual items exist and of even greater interest and profit to know the extent of the variations. One further characteristic is worth considerable note because it answers the frequent statement that merchandise sold at cut prices is bait merchandise and composed primarily of loss leaders.

In all of the investigations so far made, the conclusion is that the most profitable items are those which are sold in large volume and in which, therefore, it is easy to obtain a rapid turnover. Gross margins and even net profits per item are usually less for this class of merchandise, but the much larger volume of sales and the rapid turnover prove to be more than sufficient to overcome this disadvantage. The merchandise which is chosen for selling at cut prices is, of course, merchandise of wide appeal and, therefore, merchandise which can be sold in large volume with rapid turnover.

The many valuable investigations which have been made of average costs of doing business in various manufacturing, wholesale and retail lines have contributed greatly to an understanding of what distribution costs are and the totals they reach in various kinds of businesses. The organizations which have sponsored these studies would be the last to urge, however, that their results constitute the end of the road.

Calculation of distribution costs on individual items occupies a position in relation to these general studies of distribution costs analogous to that of production cost accounting and general accounting. With distribution costs to-day composing the largest single item in the price consumers pay for merchandise, the reason for the steadily increasing interest in individual distribution costs is clearly evident.

A FEW OF MANY HISTORIC AND INTERESTING PLACES OF BALTIMORE, THE A. PH. A. CONVENTION CITY.

The points following are within four blocks or less of Washington Monument, the first monument erected to the "Father of Our Country," located at Charles and Monument Streets. In the immediate vicinity of the monument are:

The Peabody Institute, school of music, art, library, statuary and paintings—Monument and Charles Streets. Statues of George Peabody—Mt. Vernon Place; Chief Justice Roger Brooke Taney, General John Eager Howard—Washington Square (Charles Street and Madison); Severn Teackle Wallis—Washington Square near Center Street. Mt. Vernon M. E. Church—Northeast corner Monument and Charles Street (Mt. Vernon Place). Attached to the wall of this building is a tablet bearing the following inscription: "Francis Scott Key, author of 'The Star-Spangled Banner,' departed this life on the site of this building, January 11, 1843." Walters Art Gallery—The finest private art collection in America—Northwest corner Charles and Centre Streets. Roman Catholic Cathedral—Cathedral and Mulberry Streets. The late Cardinal Gibbon's residence—Charles and Mulberry Streets.

Other locations will be referred to in succeeding issues of the JOURNAL.

NOTICE FROM TRANSPORTATION COMMITTEE.

After several months of negotiations, we have just received notice that reduced fares to the Baltimore meeting will be allowed on the certificate plan, with a smaller number of required certificates than in the past, and the time for beginning the return journey on the reduced rate tickets has been extended through May 17th, to allow members to attend the United States Pharmacopœial Convention. Further details will be given later.

THEODORE J. BRADLEY, *Chairman.*

THE DEPARTMENT OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY

President, John A. J. Funk, Galveston, Ind. J. W. Gayle, *Treasurer*, Frankfort, Ky. Chairman of Executive Committee, John Culley, Ogden, Utah. *Secretary*, H. C. Christensen, 130 N. Wells St., Chicago, Ill.

ACTIVE MEMBER STATES.

Alabama	Indiana	Montana	Rhode Island
Alaska	Iowa	Nebraska	South Carolina
Arizona	Kansas	Nevada	South Dakota
Arkansas	Kentucky	New Hampshire	Tennessee
Colorado	Louisiana	New Jersey	Texas
Connecticut	Maine	New Mexico	Utah
Delaware	Maryland	North Carolina	Vermont
D. of Columbia	Massachusetts	North Dakota	Virginia
Florida	Michigan	Ohio	Washington
Georgia	Minnesota	Oklahoma	West Virginia
Idaho	Mississippi	Oregon	Wisconsin
Illinois	Missouri	Pennsylvania	Wyoming

SUPREME COURT UPHOLDS NORTH DAKOTA PHARMACEUTICAL ASSOCIATION.

The right of a state pharmaceutical association to virtually make appointments on the board of pharmacy through its recommendatory power has been upheld by the Supreme Court of North Dakota, in the decision recently given in the case of L. Rosoff *vs*. the Pharmacy Board.

In August 1926, the North Dakota Pharmaceutical Association selected the name of P. H. Costello from a list of three submitted by a committee, as its recommendation for appointment to succeed W. P. Porterfield, whose term was to expire May 1927. The Governor, ignoring the recommendation, appointed L. Rosoff, whose name did not even appear on the recommendation list submitted by the committee. He was refused recognition by the Board and W. P. Porterfield continued to serve until his successor could legally qualify. The lower courts upheld the Governor's right to appoint outside the association's recommendation and the case was appealed.

The fact that the Supreme Court reversed the decision and upheld the pharmacy board and the state association is a tremendous victory. Other states with similar laws that have sometimes doubted the legality of this provision will find their positions strengthened by this decision.

The Fargo Forum in commenting editorially on the decisions says:

> "In making its decision, the Supreme Court undoubtedly took into consideration the intent of the Legislature in passing the law creating a pharmacy board. In this case, as in similar laws, it is much easier to determine legislative intent than it is in many others. *Because pharmacy is a highly specialized profession, calling for exacting training and examination before being permitted to practice*, the Legislature decided that the North Dakota Pharmaceutical Association, looking to the best interests of the drug business, was in better position to recommend competent board members than the Governor to select them. It did the same with other professional examining boards. (Italics ours.)

"Inasmuch as an executive had ignored this provision of the law and had ignored the state association's recommendation, it was well to test the act. The decision ends all doubt as to the Governor's right to make such appointments except on the required recommendations."

The board of pharmacy and the state association are to be congratulated on their courage in making an issue of the point and so ably defending their rights in this test case.

AN APOLOGY.

In the article "Iowa Supreme Court Upholds Aspirin Decision," which appeared in this Department in the January JOURNAL, the statement was made that this was the first state Supreme Court decision upholding an attorney general's opinion limiting the sale of aspirin to pharmacists.

This was an inadvertent error, as the Minnesota Supreme Court rendered a similar decision in July 1927. In fact, full details were supplied to the N. A. B. P. central office at that time and an article appeared in the August 1927 JOURNAL, in which the Attorney General's opinion and the Minnesota Supreme Court decision upholding the same were published in full.

Apologies are made to the Minnesota Board of Pharmacy and especially to Secretary J. W. Dargavel, whose painstaking work was of great value in bringing about the first favorable Supreme Court aspirin decision. Naturally, the Minnesota decision was of considerable help to Iowa and Secretary Dargavel also furnished considerable data to the Iowa Board for use in the case. With two states confirming this decision, there should be no difficulty in enforcing similar rulings in other states.

DISTRICT SIX MEETING IN SAN ANTONIO.

A joint meeting of the board and faculty members of District No. 6 (Arkansas, Kansas, Missouri, Oklahoma and Texas) was held at the Plaza Hotel, San Antonio, Texas, on January 24, 1930. Chairman C. B. Allison of the Texas Board presided as the N. A. B. P. vice-president and chairman of the district. Mac Childs of the Kansas Board served as recording secretary.

The meeting was unusually well attended, the Kansas, Oklahoma and Texas boards having 100% representation, Arkansas also was represented. Regret was expressed over the fact that neither the Missouri board nor colleges had sent delegates. Dean D. B. R. Johnson of the University of Oklahoma and Dean W. F. Gidley of the University of Texas represented the American Association of Colleges of Pharmacy. Secretary Christensen of the N. A. B. P. extended greetings.

An interesting address "Eighteen Years a Member of the Texas Board of Pharmacy," by John A. Weeks, was greeted with much applause.

Following the usual custom for district meetings, each board presented a set of examination questions on an assigned subject and these were criticized and commented upon from the floor. Among the several topics discussed were the recognition of colleges of pharmacy; the reciprocal recognition of pharmacists registered by territorial or district boards or at the time of creation of state boards; and the question of extending reciprocity to an applicant who has failed in examination before the board to which he is applying.

The following resolutions were presented by the Resolutions Committee, consisting of Booker Latimer of Arkansas, *Chairman*, Dean D. B. R. Johnson, and Percy S. Walker of Kansas; and were adopted:

Be It Resolved: I. *That* the chairman of the district be authorized to appoint a committee to work out a plan for a clearing house of state board examination questions for reviewing these questions and making criticisms and suggestions. The purpose of this proposed plan is to enable the board members of District No. 6 to prepare more uniform and practical examinations. This data is to be compiled in multigraphed form each year, and a copy distributed to each board member in the district and to the chairman of the N. A. B. P. Advisory Examination Committee.

II. *That* we recommend that a maximum dose of potent drugs be included in the 11th revision of the U. S. Pharmacopœia beyond which the physician shall not go without indicating, by writing the amounts in both metric and apothecary system, that he realizes and accepts the responsibility for the larger dose.

III. *That* a publicity committee be appointed at the 1930 national conventions, consisting of one member of the N. A. B. P. and one member of the American Association of Colleges of Pharmacy from each of the nine districts, as divided by the N. A. B. P., the committee to elect its own chairman, and present plans and means of putting them into effect at the 1931 national conventions for adoption.

IV. *That* the state boards of District No. 6 make it a point to inform their Senators and Representatives of the fairness of the Pharmacy Corps bill and urge support of this proposed legislation.

V. *That* the members of the National Association of Boards of Pharmacy and the American Association of Colleges of Pharmacy of District No. 6 here present extend to the San Antonio Retail Druggists Association their heartfelt thanks for the hospitality shown, including the wonderful banquet, all of which was an inspiration and was keenly enjoyed.

Other districts are planning meetings, some of which will have been held before this issue is published. Among these are a meeting of District No. 2 at Washington in March, District No. 4 in Minneapolis in February and a meeting of District No. 5 some time in March.

Word has come just before going to press that District No. 1 held a very successful meeting in Boston, Mass., on January 28th, with an attendance of twenty-five representatives from boards and colleges. This is the first meeting held by that district in ten years. Maine was represented by two delegates, Vermont by five, New Hampshire by one, Massachusetts by four, Rhode Island by five and Connecticut by four. All three colleges in the district were represented.

STATE BOARD NEWS.

Kentucky.—At the meeting of the Kentucky Board of Pharmacy held in Covington on January 14th, sixteen applicants for registered pharmacist were examined, and six passed; eleven for the assistant were also examined, and eight passed.

The following qualified for registration by reciprocity: Will D. Russell, from Georgia; Roy W. Willis and Maurice Charkine, from Ohio; Harry R. Bobst, from New Jersey; Barton N. Funderberg, from Mississippi; and Raymond Morris, from Michigan.

The next meeting of the board will be held in Danville on April 8th.

At the meeting just held, Gelon R. McGinnis, of Louisville, qualified as the newly appointed member of the Board, succeeding William Votteler, of Louisville, whose term expired recently.

Minnesota.—Six pharmacists have been granted registration as a result of the January 16th meeting.

Miss Marie A. Piesinger of Northfield, Minn., was elected president of the board of pharmacy for the ensuing year, and John W. Dargavel of Minneapolis was reëlected secretary. Miss

Piesinger holds the honor of being the second woman in the country to hold the presidency of a board of pharmacy. Miss Kittie W. Harbord of Salem was president of the Oregon Board way back in 1911.

New Jersey.—The following resolutions were adopted at the January meeting of the New Jersey Board:

Resolved that it is the sense of the Board of Pharmacy of the State of New Jersey that approval of the four-year course in Pharmacy shall be confined to such courses and institutions as will recognize the need for fundamental training in Physics, Chemistry and Biology, on which a proper technical course in Pharmacy may be built, and

Resolved further that it is the sense of this Board that a cultural background in the form of courses in English, some phases of history, economics and one or two modern languages, is a necessary part of a proper course in Pharmacy leading to a baccalaureate degree. It is also the opinion of this board that a four-year course in Pharmacy leading to a bachelor's degree, and embodying the principles set forth in the foregoing resolutions, cannot be taught on a three or four day per week schedule, but will require distribution over a full week, so as to avoid crowding of class schedules and provide time for outside study and reading on the part of the student.

Resolved that in crediting practical experience the time spent by a regularly enrolled student in a course in Pharmacy approved by this Board shall be computed on the basis of eight months credit for each college term if the net period of instruction amounts to at least thirty-two weeks per term and if the instruction given is spread over more than three days per week, and

Resolved further that in connection with credit for college work allowed on the foregoing basis, no credit shall be given for work in a pharmacy which is concurrent with attendance at college.

The maximum practical experience allowance which can be credited for attendance at a college of pharmacy under the Pharmacy Act is twenty-four months toward the "Registered Pharmacist" requirement and twelve months toward the "Assistant Pharmacist" requirement.

Pennsylvania.—Due apology is made here for an error in the January JOURNAL, in which the statement was made that "eight out of a class of 146 have been registered as pharmacists as a result of the October examination." This should have read "*eighty* out of a class of 146" and we are sorry the error was not caught in reading proof.

Wisconsin.—As a result of the quarterly examination held in January, 44 out of a class of 137 candidates were successful in receiving licenses, 31 being granted the registered pharmacist certificate and 13 the assistant license.

The next meeting will be held in Madison on April 21, 1930.

A DRUGGISTS' LEGION POST HAS OPPORTUNITIES FOR COÖPERATIVE WORK.

Chicago will have an American Druggists' Legion Post, which organization will honor President Walter A. Harris, of the Chicago Retail Druggists' Association on February 24th. The enthusiasm of A. Gorod in the post is expressed by his invitation to former service men who are druggists to join him and others at luncheon for the discussion of activities; among many others interested in the organization are O. U. Sisson, Harry Moyer, Charles L. Reynolds, Ben Friedlander. Dr. Farrell, Chicago Medical Post Commander for the past two years, has suggested occasional meetings of pharmacists with medical men of the service; the post of which Dr. Farrell is the head has about 400 members.

Every encouragement should be given the movement, not only because of the opportunities for fraternal relations, but for service. Discussions among pharmacists, and pharmacists and doctors will lead to betterment in the Government Service in which these professions are concerned, and secure deserved recognition, therefore, it is to be hoped that the idea will take hold in all sections of the country, that posts will be established in the larger cities, and the important thought kept in mind that the effectiveness of the work depends upon coördinated coöperation.

The Chicago proposal brings to mind that the Service Roll of Illinois pharmacists lists 700 names. (See JOUR. A. PH. A., 8 (1919), 1081.) We have in mind, among other opportunities, the establishment of a Pharmacy Corps, provided for in S. B. 3211 and H. B. 8473.

NARCOTIC LEGISLATION.

COMMENTS ON TENTATIVE DRAFT OF THE NEW PORTER NARCOTIC BILL.

At the recent meeting of the National Drug Trade Conference two proposed measures dealing with narcotics were considered.

One was a proposed Uniform State Narcotic Act intended to bring about greater uniformity in the legislation of the several states and to make it conform more closely with the Federal law. The committee provided by the Conference to consider this proposal has not submitted its report and apparently this legislation will not be rushed.

The other was a proposed bill by Representative Stephen B. Porter providing for a separate Bureau of Narcotics in the Treasury Department, a Commissioner of Narcotics and the licensing of all those connected with the legal use of narcotics and making other changes in the administration of the Harrison Act. A committee provided for by the Conference conferred with Representative Porter and at his request submitted certain observations and suggestions to him, as follows:

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(1) From the title of the bill and from paragraph A of Section 3 it is evident that the bill is predicated upon the treaty-making power of Congress. Under the present Harrison Act, based upon the authority of Congress to lay and collect taxes, the administration of the law can be kept within reasonable bounds so far as the constitutional rights of physician and pharmacist are concerned. A law based upon the treaty-making power would give the Federal Government a wider scope of action and its executive agents would be released from certain constitutional restraints to which they are subject in the administration of the Harrison Act.

(2) The control of the improper use of habit-forming drugs in the United States is far in advance of the degree of control exercised by any other government party to The Hague Treaty of January 23, 1912. Therefore, there can be no special obligation under The Hague Treaty to take any additional steps toward the control of such drugs unless it be assumed that the U. S. Government is morally responsible for the abuse of habit-forming drugs throughout the civilized world.

(3) The bill is objectionable in that it is intended to create a new federal bureau with a commissioner, assistant and deputy commissioners and other agents, involving a large addition to the number of federal employees and a consequent multiplication of expenditures. The entire personnel of the present narcotic service numbers something like 375 individuals, which thus far has been found ample to discharge the work entrusted to that service. Under the proposed new bureau the personnel would be at least doubled or trebled.

It is the evident purpose of the present Administration to relieve the Prohibition Bureau of a large portion of the activities it has hitherto exercised, in which case the existing Prohibition Bureau will have still more ample time to devote to the administration of the narcotic law.

(4) The proposition to abolish the existing Federal Narcotic Control Board and to substitute three medical officers designated by the Surgeon-General of the Public Health Service does not seem to be justified. The present Board has functioned in a highly satisfactory manner and there is no substantial evidence to sup-

port any claim that narcotics have been admitted through the Custom House in excess of the amounts properly necessary for legitimate medical use.

The new method of control proposed is also defective in that it does not provide for a representative of pharmaceutical interests, since many of the problems relating to the importation, manufacturing, the keeping of proper reserves and the distribution of narcotic drugs to the wholesale and retail drug trade, to hospitals and to the medical profession involve technical questions with which no physician can be familiar. Only through the presence of a representative of pharmacy upon such board of control can such questions be given the intelligent and technical consideration which they deserve.

(5) Under the existing Harrison Act the means of control through the registration of manufacturers, producers, dealers and physicians, and the use of duplicate order blanks permits every ounce of a habit-forming drug to be traced from its entry through the Custom House to its final consumption for medical purposes, and there is no substantial evidence tending to show that there is or has been any material leakage of habit-forming drugs from the channels of legitimate consumption provided by the law. The effect of the Porter Bill, therefore, should it become a law, would be simply to provide more cumbersome and more expensive machinery for supervision of that portion of the drug traffic which is already properly controlled, and to place additional burdens upon physicians and pharmacists.

(6) The bill is defective in that it does not provide any means for the more effective control of habit-forming drugs which are introduced by smuggling. All the available evidence indicates that practically all of the habit-forming drugs distributed for illegitimate purposes are obtained through smugglers, and that no material portion of them is derived from the quantity which comes through custom houses and which is distributed through pharmacists and physicians.

(7) The present Federal Narcotic Act is one of the most efficiently enforced and one of the best observed laws upon the federal statute books. The official records at Washington disclose the fact that less than one per cent of the offenses against the Narcotic Act are committed by physicians and pharmacists, and of this small number of offenses the majority are of purely technical character, such as errors in the keeping of records, the dispensing of narcotics upon a physician's prescription when, under the Regulations, an Order Blank should have been used, etc.

(8) The last paragraph of Section 3 is highly objectionable in that its apparent intention is to deprive citizens from the opportunity of having a court review of the decision of the Commission either with respect to the granting of licenses or their revocation. Ample experience with government officials in the enforcement of the Prohibition Act and other federal laws has proved the absolute necessity of the possibility of judicial review as a restraining influence upon arbitrary administrative action. If the decision of an administrator is within the scope of his authority as defined by law the possibility of judicial review cannot interfere with the effectiveness of his execution of the law. On the other hand, if his ruling is not within the law there is no means whereby the injured can obtain redress except through the medium of judicial review. This attempt to do away with the right of a court review of executive action should, therefore, be resisted to the utmost.

(9) It is questionable whether the licenses proposed to be issued under paragraph B of Section 3 would not constitute an invasion of the rights reserved to the states. The section is also defective in that the language "the applicant or licensee is not otherwise a fit person to possess a license," is highly indefinite and would seem to make the mere will of the Commissioner of Narcotics the sole test as to whether a license should be granted or withheld. The language of the bill is in other respects indefinite and lacking in that certainty of meaning which should obtain in a statute, the effect of which may be to deprive citizens of their property or liberty.

Mr. Porter introduced his measure in Congress on January 23, 1930, in two bills, H. R. 9053 and H. R. 9054 (see copy of the Porter Bills under "Legal and Legislative" in this issue of the JOURNAL), the former being referred to the Committee on Ways and Means and the latter to the Committee on Foreign Affairs. Two important modifications were made in the proposed legislation, prior to its introduction, in response to the suggestions of the Conference Committee. The language "the applicant or licensee is not otherwise a fit person to possess a license" has been eliminated as a basis for the refusal to issue a license or for the suspension or revocation of a license, the grounds now being "(1) the applicant or licensee is a narcotic drug addict, or (2) the applicant or licensee has been convicted of violating the law of any state or of the United States relating to narcotic drugs." Provision is made for appeal to the U. S. Courts by any one who is denied a license or whose license is suspended or revoked by the Commissioner of Narcotics after a hearing before the Commissioner or any officer or employee of the Bureau designated by him.

Since all branches of Pharmacy are giving satisfactory coöperation, and since the results so far as the legitimate use of narcotics is concerned are satisfactory, it does seem reasonable to expect that any additional legislation deemed necessary shall be limited to curbing illicit use, and that further burdens should not be imposed upon those who have been given the duty of preparing, distributing and dispensing these very necessary substances.

PHARMACIST CANNOT ANALYZE LIQUOR SAMPLES.

A recent ruling of the Enforcement Bureau of the Treasury Department informs that "the possession of any liquor other than that received by the pharmacists pursuant to properly approved permit to purchase would be possessed illegally. It would appear that the proper place for analysis of intoxicating liquors for the purpose of determining the presence of extraneous matter would be either the city chemist, the chemist of the Health Department, or the State Chemist of the locality in which the physician is practicing." From the foregoing it seems that the Bureau considers possession of intoxicating liquors for the purpose of analysis by others than officials illegal.

There seems to be no reason why any pharmacist or chemist should not be permitted to analyze medicinal liquor (legal).

INDIANA LAW TAXING CHAIN STORES IS DECLARED TO BE UNCONSTITUTIONAL.

The Indiana chain store tax law is unconstitutional, the District Court for the Southern District of Indiana has held. (See JOUR. A. PH. A., 18 (1929), 92.) The law makes an unreasonable and arbitrary classification, the court ruled, pointing out that the plaintiff in the case operates 225 grocery stores in the city of Indianapolis and would pay a total tax of $5443, whereas other firms in the State with but one store would pay only $3.00, although having a much larger investment and income than the plaintiff.

The law cannot be sustained under the police power of the State, the court held, because it does not relate to the public health, the public welfare, the public morals or the public safety.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

At the last meeting of the American Association of Colleges of Pharmacy, there were quite a number of papers presented before the Pharmacy Section on the subject of the prescription. I have decided to run those papers in a consecutive series so that they will form a sort of symposium on prescription work. The following on "Finishing the Prescription" by Dean Newton is one of the series.—C. B. JORDAN, *Editor.*

FINISHING THE PRESCRIPTION.

BY HOWARD C. NEWTON.*

The most evident and therefore the most common criterion for judging the care with which a prescription has been compounded is the physical appearance of the finished product. Not only the layman but the physician, the nurse and even other pharmacists, are influenced largely in their opinion of the excellence, or lack of excellence, of a compounded prescription by the manner in which it is dispensed. In teaching students to dispense prescriptions we must not ignore these facts. It would, indeed, be difficult to devote too much time in our classes to this important subject of putting the finishing touches upon the products of the prescription counter. The compounding of physicians' prescriptions is the fundamental function of professional pharmacy and it is the one phase of the practice of pharmacy, the duties and privileges of which are universally restricted by law to the pharmacist. The welfare of the public demands that restriction. Since the compounding of prescriptions is looked upon by the public as a highly professional practice, differing greatly from the many other phases of his work, it would seem proper that the pharmacist should make the products of this practice highly distinctive, differing markedly from all other materials that he may distribute. I believe that you will agree with me in this thought and yet when we see the products of some prescription counters we cannot but wonder why those pharmacists should take so little care in the finishing of their prescriptions. It almost seems as if they were purposely trying to avoid the enjoyment of one of the chief advantages of pharmacy—the professional atmosphere which places it above the rank of a trade.

For those who may be inclined to doubt the extreme importance of the physical appearance of the compounded prescription I will make this statement: the most successful prescription stores of this country are those in which the details of finishing the products of their prescription counters are the result of much study and the execution of these details is a matter of continual concern. To prove this I have gathered specimens from successful stores throughout the country, illustrating the care which these stores give to the finishing of their prescriptions. For the purposes of this discussion I shall divide the finishing of a prescription into the following elements:

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* Dean, Creighton University College of Pharmacy.

1.—The choice of the container and the type of closure.
2.—Labels.
3.—Special finishing touches such as capping, sealing, etc.
4.—Wrapping.

Let us consider these four elements with respect to the dispensing of the several forms of prescriptions. I shall endeavor to state briefly the possibilities under each heading and my own preference in selection, leaving opportunity for criticism and general discussion.

LIQUIDS.

1.—As a container for the liquid prescription we may choose from a great variety of types of bottles, round, square or oval, graduated or ungraduated, flint, amber, or blue, imprinted or plain. Then for the closure we may have a cork stopper or one of the many kinds of metal caps. Bearing in mind that favorable distinction is our object, I would select an ungraduated, flint-glass bottle, imprinted with the name of the store, with a good sound cork as the closure. I reject the graduated bottle because of its evident inaccuracy and the inference that might readily be drawn from it to the effect that the compounder used it as a graduate in his work. I prefer the cork stopper rather than the other forms of closures because it is equally efficient and has the advantage of being distinctive—so many proprietary products are using the other forms of closures. Then, too, the neck and lip of the cork-stoppered bottle are better to pour from than those of bottles specially molded for other closures.

The bottle should be perfectly clean and always polished with a cloth before being labelled in order that it may radiate quality. The mouth of the bottle should be cleaned before the cork is inserted. New bottles should be used for all prescriptions or, in the case of refills, the old bottle may be thoroughly washed and rinsed with distilled water, if it is to be used again. The type of bottle selected, round, square or oval, should be reserved exclusively for prescriptions—other types being used for all other orders. For eye washes it may be desirable to have the smaller sizes of the standard bottle made with wider mouths for the convenient use of medicine droppers, or, a special dropper bottle may be employed. In the case of collodions, liquid caustics and similar local applications, it is desirable to use applicator bottles.

2.—The label on a prescription serves to indicate to the patient the way he is to use the medicine. It is also an advertisement of the store in which the prescription was compounded. Therefore, for the benefit of the patient, it must be perfectly legible; it must be neat, pleasing to the eye and consistent with the dignity of a profession if it is to be a good advertisement for the store. The typewriter has aided greatly in making it possible for all to have perfectly legible labels and most stores have taken advantage of it. The size of the label, whether it shall be the standard or blanket, and its position on the bottle, whether it shall be placed close to the top, in the center or near the bottom of the front of the bottle are matters to be decided. I prefer a label of the next size above the standard, placed relatively high upon the bottle. I reject the blanket label because it obscures the contents of the bottle (although that may be desirable at times). The label should be placed upon the bottle carefully in order that it shall not be crooked.

A crooked label gives an appearance of carelessness, exactly the opposite of what is desired. Auxiliary labels—shake, external, poison, narcotic, caution, etc., should be of a size and shape to conform to the main label. The position of these is determined by the shape of the bottle used and its size. I teach, that of the auxiliary labels for prescriptions, the poison label belongs to the physician and is to be used only on his specification; the shake label, the external use label and others, are the property of the pharmacist and are to be used at his discretion. A valuable auxiliary label for eye washes is one with the inscription, "this medicine is for the eyes" or some similar inscription. The proper use of auxiliary labels is an important factor in dispensing.

3.—In dressing up the bottle we find many ideas expressed. Fluted caps, viscose caps, wax seals, parchment paper coverings and similar devices are illustrated in the specimens that I have gathered from many stores. All of these are excellent and serve to make the prescription distinctive and also to assure the patient that the bottle has reached him in an untampered condition. I believe we should teach our students to make the most of such inexpensive means of making their prescriptions appear to be the work of real craftsmen.

4.—Wrapping is a process that should not be neglected. All packages from the store should be wrapped so as to uphold the tradition that the pharmacist has for being the one who can do this as it should be done. It is good advertising and not expensive. Either twine or adhesive tape may be used to secure the paper and I would suggest that one be used for prescriptions and the other for general packages in order to distinguish them. In most stores under such a plan, the twine would be reserved for the prescription package. One store from which we have a specimen uses sealing wax to secure the paper of small prescription packages. You will note that at least one of these specimens from fine stores has a wrapping paper marked especially for his prescription packages. It has doubtlessly proved to be worth while and is certainly attractive. The teacher who belittles the pharmacy course in which package wrapping is taught does not realize the value of the art, yet, I have come in contact with such teachers in our Association meetings. I believe that wrapping the package properly is a part of dispensing the prescription.

CAPSULES, POWDERS, PILLS AND TABLETS.

1.—For capsule containers we have a choice of one of several types of boxes or a special glass vial. Both the hinged-cover shoulder box and the special vial are popular and practicable.

For divided powders, or papers, a box is the only container suitable and the choice is merely of the type to use—telescopic, shoulder or hinged shoulder (a sliding box is generally considered out of the question).

Bulk powders are often dispensed in round or square utility cartons but the screw-capped, wide-mouth bottle or jar is usually preferred. A special sifter-top carton is the preferred method of dispensing dusting powders.

Pills and tablets are well dispensed in boxes or vials. The box is the more popular container.

2, 3, 4.—The labels, special touches and wrapping of these forms of prescriptions conform to the observations made under the heading "liquids." In

the case of the use of the vial for capsules, careful arrangement of the capsules in the container is a factor that makes the product more attractive. In cases where there are many divided powders or papers, in a box, it may be well to separate them into small bundles by tying with narrow ribbon or with thread. This keeps them in a tidy condition until used.

OINTMENTS.

1.—The proper container for the ointment is undoubtedly a jar or tube. The jars may be opal or amber, tall or short, with aluminum or nickled covers. The opal jar is, I believe, the most satisfactory and the tall form is the more convenient, especially in the smaller sizes as it offers a better space for the label on the side of the jar. Tubes are a sanitary means of dispensing ointments and are most desirable for ophthalmic ointments.

2.—Upon ointment jars the standard prescription label may be used. On tubes it is advisable to have a special label that completely encircles the tube in order to insure that the label will adhere to the tube as it is used. A carton for the tube and a secondary label on it is one good method of caring for the labelling of a tube.

3.—In using ointment jars it is best to carefully wipe out the cover of the jar as well as the jar itself before placing the ointment in it. There is usually dust in the cover which, if not removed, will fall upon the ointment. The surface of the ointment in the jar should be slightly concaved so that it will not adhere to the cover. A strip of cellophane or other transparent material attached around the jar and over the label will be found to be a simple and attractive means of protecting the label from grease spots and dust.

4.—No special wrapping is required for ointment jars.

SUPPOSITORIES.

1.—It seems wise to have a special container available for suppositories. A box, divided into compartments and imperviously lined, is a standard container and is very satisfactory. In the absence of this special container an ordinary powder box may be used and the suppositories individually protected by wrapping in waxed paper.

2.—A special label calling attention to the necessity of preserving the suppositories in a cool place is almost a necessity.

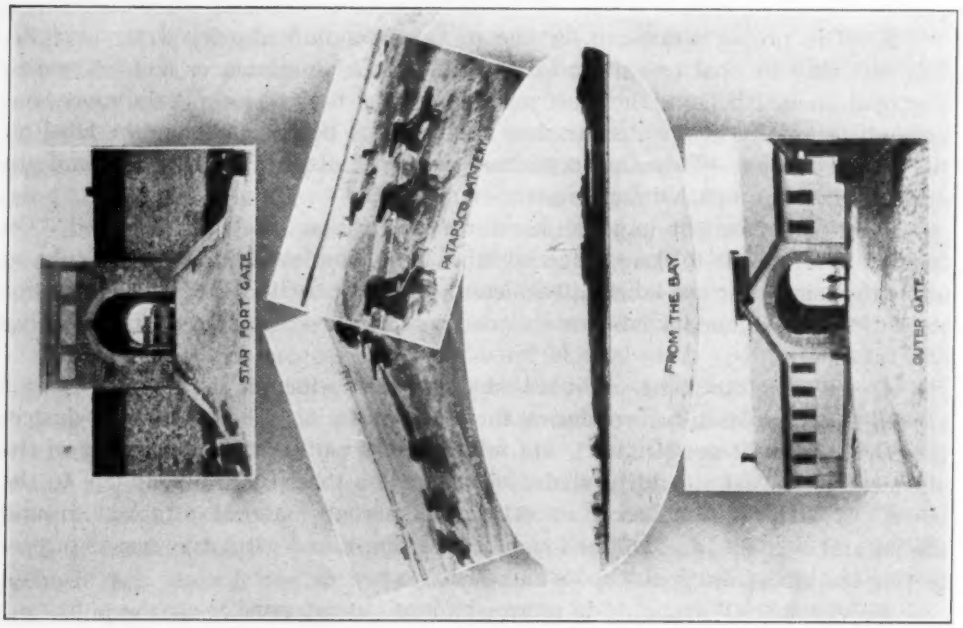
3, 4.—No special requirements need to be observed.

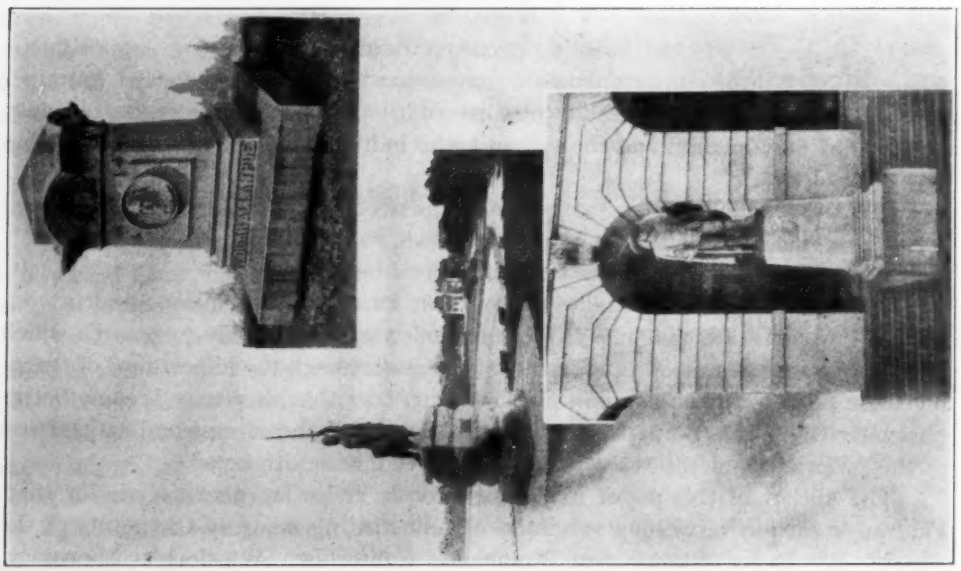
We have now covered the more common forms of prescriptions and in conclusion I would state that my purpose in reviewing these many facts with which you were probably already familiar is to impress you with the importance of teaching these facts to the students in pharmacy in order that they may become better pharmacists. Then, perhaps, they will share some of the success and satisfaction of the proprietors of the stores whose products I have displayed.

The author of this paper is indebted to the following pharmacists for their kind assistance in furnishing specimens for illustrating many of the points of the paper: W. Bruce Philip, San Francisco, California; Whitlock's Pharmacy, Spokane, Washington; J. Leon Lascoff & Son, New York, N. Y.; A. J. Affleck, Sacramento, California; Hilton's Ethical Pharmacy, Washington, D. C.; The

Owl Drug Company, San Francisco, California; J. G. Godding & Co., Boston, Mass.; Bowerman's Pharmacy, San Francisco, California; Leonard E. Seltzer, Detroit, Michigan; W. A. Piel, Omaha, Nebraska; and Frates & Lovotti, San Francisco, California.

BALTIMORE—THE A. PH. A. CONVENTION CITY—Views at Fort McHenry.





Monuments over the graves of Edgar Allan Poe, Severn Teackle Wallis, Lord Baltimore (Cecilius Calvert).

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meetings of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

BALTIMORE.

The January meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Emerson Hotel on Friday, January 31, 1930, President Frank L. Black presiding.

Herman Mendelson, violinist, and Salvatore Molinari, pianist, entertained with musical numbers, including a composition by Mr. Molinari dedicated to the Kappi Psi fraternity.

R. E. L. Williamson was the speaker, and had as his subject—"The Independent Retail Druggist." Mr. Williamson enumerated statistics showing the number of independent retail druggists in Maryland, also in the United States, the amount of money invested in the retail drug business, and the service the independent druggist is rendering to the general public. He compared the opportunities of the independent druggist to give personal, painstaking service, with the lack of such opportunities in the service of the incorporated, soulless, chain stores. He, however, urged the independent retail druggists to adopt up-to-date advertising and display methods. He also pointed out some of the benefits that the independent druggist may derive through the better selection of goods, rapid turnover of stock and the elimination of slow-selling or unsalable stock. He further stated that the general public is interested in odd prices, as well as in bargain or cut prices, and suggested that the wide-awake independent druggist note this tendency and adopt odd prices for certain articles.

Mr. Williamson enumerated the different studies and investigations that are being conducted by the Federal Government and by different pharmaceutical groups in the interest of independent druggists. He also mentioned some of the laws that have been proposed and urged for passage that are of interest to the independent druggist. In conclusion he referred to the bright outlook for independent pharmacists.

President Black announced George Frederick Schmidt, Jr., as the recipient of the second annual award by the Baltimore Branch of one year's membership in the AMERICAN PHARMACEUTICAL ASSOCIATION, to a student of the School of Pharmacy of the University of Maryland.

The report of the Treasurer showed the Baltimore Branch to be in a healthy, progressive position. Reports were received from the chairmen of the different standing committees, including a comprehensive report from Dr. Glenn L. Jenkins, chairman of the Committee on Science and Practice of Pharmacy, and a very interesting report from Dr. A. G. DuMez, chairman of the Committee on Education and Legislation.

The Committee on Nominations suggested the reëlection of the present officers, and the following were therefore, declared elected for the year 1930:

President, Frank L. Black, 2839 W. North Ave., Baltimore Md.; *Vice-President*, Aquilla Jackson; *Secretary-Treasurer*, B. Olive Cole, Green & Lombard Sts., Baltimore, Md.

Committee on Membership: *Chairman,* Lawrence L. Miller; Mrs. Anna C. Norton; Aquilla Jackson. **Committee on Professional Relations:** *Chairman,* E. G. Eberle; Lloyd N. Richardson; L. M. Kantner. **Committee on the Science and Practice of Pharmacy:** *Chairman,* Glenn L. Jenkins; Wm. J. Lowry, Jr.; John C. Krantz, Jr. **Committee on Education and Legislation:** *Chairman,* Dr. A. G. DuMez; R. L. Swain; P. I. Heuisler.

B. OLIVE COLE, *Secretary-Treasurer.*

CHICAGO.

The 187th meeting of the Chicago Branch of the A. PH. A. was held Tuesday evening, January 21st, at the Illinois School of Pharmacy. The meeting was presided over by President Lindahl. The report of the Secretary-Treasurer was presented, as follows:

The Chicago Branch of the A. PH. A. held eight meetings during the past year, the 179th–186th inclusive. The programs have been diversified and very profitable. The attendance has been good but there is need of stimulating greater interest and increasing our membership. During the year 1929 twenty-two new members have been added while twenty-nine members resigned or moved away, leaving a total membership of 412.

FINANCIAL STATEMENT.

Balance, January 1, 1929	$219.67
Contributions	178.00
Commissions (New members)	22.00
Printing and Typing	$117.90
Postage	19.75
Dinners	4.00
Speakers	45.00
Phone and Telegrams	1.75
Refreshments	25.70
Cash on hand, January 1, 1930	205.48

Respectfully submitted,

S. W. MORRISON, *Sec.-Treas.*

Dean Day expressed the regret of President Christensen of his inability to be present at the meeting. Three members of the revision committee of the N. F., Dr. Fantus, Mr. Becker and Prof. Gathercoal, were present and Chairman Gathercoal, of the revision committee, spoke a few words in behalf of the committee.

Mr. Gray presented the following report of the Committee on Nominations. The nominees were duly elected by an unanimous ballot:

President, J. A. Hynes; *First Vice-President,* R. E. Terry; *Second Vice-President,* G. L. Webster; *Third Vice-President,* R. A. G. Linke; *Delegate to the House of Delegates,* E. N. Gathercoal; *Secretary-Treasurer,* L. E. Martin. *Committee Chairman: Membership,* C. P. Van Schaack; *Legislation,* J. Riemenschneider; *Practice,* I. A. Becker; *Medical Relations,* Dr. Bernard Fantus; *Publicity,* Samuel C. Henry.

Dean Day moved that a rising vote of thanks be given to the retiring officers.

President-elect Hynes introduced the speaker of the evening, Dr. C. E. Bills, of Mead, Johnson & Co., who spoke on "Irradiated Ergosterol."

The production of artificial vitamin D was first made by Dr. Thompson in 1854, who exposed cocoanut oil to the sun's rays and found the oil to be beneficial in tuberculosis. Dr. Steenbock, over ten years ago, studied the effect of sunlight on the growth of goats. In Europe, over twenty years ago, cod liver oil was used on patients with rickets and the ultraviolet rays were tried on the patients then with beneficial results.

In 1924 Dr. A. Hess found that oils exposed to ultraviolet light had increased antirachitic properties. Steenbock, at the same time exposed various foods to ultraviolet light. Cholesterol had antirachitic properties after such treatment. The lipoid fraction absorbed the ultraviolet rays.

In 1925 Dr. Hess found that cholesterol, after irradiation, gave a different picture with a spectroscope, the absorption bands had shifted to a different position. Ergosterol is present in cholesterol about $^1/_{10}\%$. In 1926 Rosenblum found irradiated ergosterol to be highly potent in vitamin D.

Ergosterol was first obtained from the fat of ergot at a cost of $200 per Gm., but at present is obtained from yeast at about 50 cents a Gm. One gram of activated ergosterol is equal to about one ton of cod liver oil in vitamin D content. The variety of yeast, amount of air and culture media, all influence the yield of ergosterol from yeast. Ergosterol is found mainly in fungi, and also found in most bacteria. Yeast is extracted with acetone or some suitable solvent, the fat saponified and ergosterol separated by fractional crystallization. Too lengthy irradiation of ergosterol produces decomposition and toxic substances, a mercury quartz lamp being used to give the ultraviolet light. Ergosterol dis-

solved in ether and then irradiated gives higher potency in vitamin D than with other solvents. Vitamin D was recently reported obtained in the pure state, $^1/_{100,000}$ mg. per day being sufficient to kill rabbits. The changes on activation are little known but the absorption bands are studied and it is found that isoergosterol, a decomposition product and ergosterol, mixed, give the same spectra picture as activated ergosterol.

Vitamin D may be another form of isoergosterol (a change in molecular arrangement) or it may be a ketone. The fact that activation may occur at temperature of liquid air is evidence of electronic change in ergosterol.

The first products received from Europe were not standardized and varied greatly in strength. In 1927, in the United States, the activated ergosterol was standardized to be 100 times and 5 times the strength of cod liver oil in vitamin D. Irradiated ergosterol when properly standardized is not toxic as commonly believed. The toxic dose is about 1000 times the therapeutic dose, when given every day on rats and the same relation seems to hold for humans. The solution of activated ergosterol keeps indefinitely if kept stoppered and free from rancidity. The blood platelet count is increased but there is no apparent increase in red blood corpuscles on administration of viosterol.

A general discussion followed the lecture and numerous questions were asked regarding viosterol. Dr. Fantus inquired regarding a method of standardization by immission of ultraviolet rays instead of the biologic assay and mentioned the advisability of adopting a suitable name for the next Pharmacopœia.

A rising vote of thanks was given Dr. Bills for his very interesting talk and the meeting adjourned.

S. W. MORRISON, *Secretary.*

DETROIT.

The December meeting of the Detroit Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held December 12th. The meeting was preceded by a dinner and was called to order by James Lidell, *Second Vice-President.* The minutes of the November meeting were read by the Secretary and approved. Chairman Burniac of the Membership Committee announced five new members, bringing his total for three months up to twenty-three.

Mr. Lidell presented Leonard A. Seltzer, the speaker of the evening. He gave a most interesting talk on the future of Pharmacy. He said that while the subject is an old one the usual way of treating it is not the right one. He said too many pharmacists expect a quick way out of difficulties by legislation. He said the physician accepts too much responsibility when he diagnoses, prescribes, compounds, dispenses and if necessary signs his own death certificate; this practice weakens his prestige and professional dignity and finally his bank account. His patients are limited to medicines on hand, rather than the products of the pharmacy. The doctor, in justice to his patient, should give him the benefit of the knowledge of the pharmacist.

Mr. Webster said that Mr. Seltzer's talk opened a large field for discussion, a program just begun by the N. A. R. D. and D. R. D. A., in an organized effort to bring back pharmacy to the drug store through U. S. P. and N. F. propaganda.

Mr. Burniac said the physician and dentist are recognizing the pharmacists who bring medicines to the front of the store. He advised the removal of the "Cut Rate" sign and display of three feature items pertaining to pharmacy each month; thereby the pharmacist can promote pharmacy.

Dr. Dikeman said the speakers had suggested good propaganda, diplomatically presented.

Mr. Webster remarked that the younger men of to-day will be leaders of to-morrow and must carry on the work started by the present generation.

W. L. Parker and James Lidell assured the members that the younger generation can be depended upon to sponsor the professional side of pharmacy.

Mr. Seltzer was given a rising vote of thanks.

BERNARD A. BIALK, *Secretary.*

NEW YORK.

The regular monthly meeting of the New York Branch, A. PH. A., was held at the College of Pharmacy, Columbia University, on January 13th. President Hugo H. Schaefer was in the chair.

The report of the Committee on Student Branches, Dr. Robert P. Fischelis, *Chairman,* was read in detail. The recommendations in the report were:

(1) "That Local Branches of the AMERICAN PHARMACEUTICAL ASSOCIATION, in cities where there are Colleges of Pharmacy, endeavor to

bring the work of the AMERICAN PHARMACEUTICAL ASSOCIATION to the attention of students in these colleges by inviting them to the Local Branch Meetings and occasionally holding meetings in the various colleges."

(2) "That prominent members of the Local Branch be made available as speakers to College Science Clubs or Fraternities."

(3) "That the Editor of the JOURNAL and the Publication Committee be requested to work out some kind of a club subscription rate whereby groups of ten or more students could subscribe for the JOURNAL at an annual rate of about Two Dollars each."

It was voted that the Committee's three recommendations be approved, and that they be sent to the Editor of the JOURNAL with the hope that he would pay special attention to Recommendation Number 3.

The following officers were elected by the Branch for the ensuing year.

President, Robert R. Gerstner; *Vice-President*, Robert P. Fischelis; *Secretary*, Herbert C. Kassner; *Treasurer*, Turner F. Currens; *Secretary of Remington Medal Committee*, Hugo H. Schaefer; *Delegate to House of Delegates*, Hugo H. Schaefer; *Chairmen of Committees: Education and Legislation*, Robert S. Lehman; *Fraternal Relations*, Jacob Diner; *Membership*, John L. Dandreau; *Progress of Pharmacy*, Reginald Dyer; *Audit*, Joseph L. Mayer.

Chairman Dyer of the Committee on the Progress of Pharmacy, read the names of some recent Newer Remedies that had come to his attention, and gave interesting abstracts on the following subjects, Digitalis, The Keeping Properties of Coca Products, Chemical Tests for Drunkenness and The Vitamin Content of Tomatoes Ripened Artificially with Ethylene.

Dr. Higgins, of the Lederle Antitoxin Laboratories, was introduced as the speaker of the evening.

The Branch listened with attentive interest to Dr. Higgins' development of his topic—"The Retailing of Biological Products." In addition to discussing the marketing of biological products in its many ramifications, he also talked about interesting and unusual facts concerning Diptheria, Toxin-Antitoxin Treatment, Antipneumococcic Serum, Puerperal Septicemia, The New Canine Distemper Serum of the British Medical Council, Convalescent Serum for Measles, Hog Cholera and Sleeping Sickness.

An interesting discussion of the paper followed during which such topics as Allergic Preparations, Asthma, Hay Fever, Protein Idiosyncrasy and the timely topic of Parrot Fever were considered.

After a rising vote of thanks was given to Dr. Higgins, the meeting adjourned.

HERBERT C. KASSNER, *Secretary.*

PHILADELPHIA.

The regular monthly meeting of the Philadelphia Branch, AMERICAN PHARMACEUTICAL ASSOCIATION was held in the P. A. R. D. Building, 2017 Spring Garden Street, Tuesday evening, January 14th, with President Hoch in the chair.

The minutes of the December meeting, presented by the Secretary, were accepted. The membership application of Harry T. Haefelin, 1420 Rush St., Philadelphia, was accepted and forwarded to the parent organization for approval. The Secretary announced that the February meeting would be of unusual interest and would be devoted entirely to the discussion of problems relative to the U. S. P. Revision. Professor E. Fullerton Cook, Chairman of the Revision Committee, will act as Chairman for the February meeting; he advised that the members should bring their suggestions and recommendations for the new Pharmacopœia in order that they may be discussed.

The feature of the meeting was the "Prescription Clinic," an annual affair of the association. Chairman Charles T. Pickett, of the Committee on Practical Pharmacy acted as chief clinician. He had a very excellent collection of prescriptions which had been selected from various drug stores in Philadelphia. The prescriptions were copied on a large chart and each was discussed very carefully as many of them involved unusual methods of compounding. The meeting proved to be one of the most interesting of its kind ever held by the association.

There was a large attendance and great general enthusiasm was displayed by the members. Following the meeting the members were served a fine luncheon in the dining room of the P. A. R. D. Building.

FRANK H. EBY, *Secretary.*

PITTSBURGH.

A meeting of the Pittsburgh Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held January 21, 1930, at the School of Pharmacy, of the University of Pittsburgh. Presi-

dent John G. Rees called the meeting to order.

Chairman Edward C. Reif of the Committee on Nominations reported the following names: For *President*, John G. Rees; *Vice-President*, Stephen Wilson; *Secretary*, Frank S. McGinnis; *Treasurer*, George B. Saylor; *Delegate to House of Delegates*, C. Leonard O'Connell.

Since there were no further nominations the aforementioned persons were duly elected and installed as officers of the Pittsburgh Branch, A. PH. A.

President John G. Rees has been singularly honored in the fact that he will have served as President of the Branch for three consecutive years.

Dr. Louis Emanuel, who for many years has represented the Pittsburgh Branch in the House of Delegates, asked to be relieved of this duty. He has faithfully and diligently served as voting delegate, and contributed greatly to the advancement of all concerned. The office vacated by Dr. Emanuel has been accepted by Dr. C. Leonard O'Connell.

This meeting was marked by the usual attendance and interest.

The speaker, Dr. A. F. Judd, professor of Materia Medica of the School of Pharmacy, presented a non-technical paper on Vitamines. The various classifications, old and new, were considered.

An informal discussion followed the main presentation. Points of interest were brought out in connection with the much discussed "Vitamines."

President Rees in his announcements stated that the February meeting of the Pittsburgh Branch will be in charge of the Pharmacy Department of the Pittsburgh College of Pharmacy.

He announced the appointment of the Committee on Program as follows: Stephen Wilson, George B. Saylor, George Wilson, Lester V. Moore.

FRANK S. MCGINNIS, *Secretary*.

MINNESOTA PHARMACEUTICAL ASSOCIATION.

The annual meeting of Minnesota Pharmaceutical Association was held in Minneapolis February 12th–14th. The Scientific Section held a joint meeting with the Northwestern Branch, A. PH. A.

Among the subjects discussed and papers presented during the joint meeting were "Subscription Pricing," by G. Bachman; Professional Ethics," by H. O. Tiegen; "Biological versus Chemical Assays," by Marvin R. Thompson; "Business Ethics," by Paul J. Binek; "Professional Standards," by K. K. Kellar; "Drug Plant Culture," by A. B. Fischer; "Determination of Permissible Dyes in Candy," by C. H. Rogers and Alice Dechter.

E. L. Newcomb was on the program for a paper and former president of the A. PH. A., D. F. Jones, delivered an address. Interesting reports were made by the several committees, among them those on "Education," and "Hospital Pharmacists."

Dean Wulling added largely to the program by the contribution of a number of reports and papers.

PHILADELPHIA DRUG EXCHANGE.

The sixty-ninth Annual Meeting of the Philadelphia Drug Exchange was held January 28, 1930, in its rooms in the Bourse Building. The Annual Report was presented on behalf of the Board of Directors and approved, and an election for officers and directors for the current year was held. The following were elected:

President, John F. Belsterling; *Vice-President*, Harrison S. Hires; *Secretary*, Joseph W. England; *Treasurer*, A. L. Hilles, Jr.; *Board of Directors:* J. Mervin Rosenberger, Benjamin S. Thorp, H. K. Hineline, Walter P. Miller, Herbert R. McIlvaine, F. L. Bodman, Walter V. Smith, Alexander C. Fergusson, Jr.

Addresses were made by Emil P. Albrecht, President of the Philadelphia Bourse, and Henry Paul Busch. Sympathy was expressed by the members on the illness of Ex-President C. Mahlon Kline, and the hope voiced that he would soon be well and strong.

Prof. Charles H. LaWall pleaded for financial encouragement in research in pharmacy schools in the following words of his report:

"As long as you are in business you will be dependent upon pharmacy. Why not help it now or provide or plan for financial help later? Thus, and thus only, will pharmaceutical research receive its due, for upon the results of pharmaceutical research many fortunes have been accumulated by those who have spurned the ladder by which they rose to affluence."

The annual banquet of the Drug Exchange was held in the Bellevue-Stratford Hotel, January 30th.

PROGRESS IN MEDICINE AND PHARMACY.*

BY JOHN F. ANDERSON, M.D.[1]

"I am glad to have the pleasure of addressing the Northern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION and of discussing before you some of the developments of the past few years in medicine and pharmacy. The practice of medicine and pharmacy is a very different thing from what it was when I graduated in medicine some 25 years ago. With a few exceptions, like quinine in malaria and mercury in syphilis, the treatment of disease was then largely based upon the empiric use of drugs or methods. The new sciences of pharmacology, biochemistry, chemotherapy, bacteriology and immunology were just coming into prominence as powerful allies and supports of scientific medicine. As a result we were acquiring our first definite knowledge of the treatment of disease based upon sound research in the laboratory and at the bedside. Since then there have been rapid strides toward the goal of the specific treatment and prevention of diseases, not only among those of infectious origin, but also among those caused by a failure of the proper functioning of the important organs of the body.

"The science of bacteriology made the first great advance in the specific treatment and prevention of disease when von Behring and Roux, following the trail so clearly blazed by Pasteur and Koch, announced the discovery of tetanus antitoxin and of diphtheria antitoxin. Before diphtheria antitoxin came into use, one in every three children who developed the disease died. Tetanus antitoxin made it possible to prevent many deaths with the horrible and painful symptoms of lock-jaw.

"The epoch-making discoveries of Roux and of von Behring opened to us the vista of the eventual control of other diseases caused by bacteria. Unfortunately, this hope has been slow in being realized. The next great advance was not made until 28 years later, when came the discovery by Drs. George F. and Gladys H. Dick of the cause of scarlet fever, its prevention, diagnosis and treatment. The Dicks' discoveries were first published in 1923, and have made it possible to apply with confidence specific means in the treatment and prevention of scarlet fever of which there occur annually in the United States more than 200,000 cases.

"It has just been stated that prior to the work of the Dicks on scarlet fever, an interval of 28 years elapsed without the discovery of a single antitoxin of major importance. During this period, naturally, an enormous amount of work was done in an effort to acquire control of scarlet fever. You wonder why all this work was sterile as far as the production of positive results, while the Dicks were so phenomenally successful, and you probably rightly suspect that they introduced a new principle or a new technical method into the study of scarlet fever. Most of the work on scarlet fever has been done on laboratory animals. The Dicks came to the conclusion that laboratory animals were not susceptible to scarlet fever. When they suspected that the cause of scarlet fever was a streptococcus, they tested this hypothesis not on guinea-pigs, but on human volunteers. They produced typical scarlet fever in a young man by spraying his throat with a streptococcus obtained from a case of scarlet fever. They thus demonstrated beyond question that a streptococcus was the cause of scarlet fever. And the same principle was used when they wished to determine whether the scarlet fever streptococcus produced a toxin. The toxin of the scarlet fever streptococcus is characterized by the fact that it is without effect on laboratory animals. In this respect it is distinguished sharply from the toxins of the diphtheria and tetanus bacilli. The standardization of the scarlet fever toxin and scarlet fever antitoxin must therefore be done by means of skin tests in susceptible human beings. This is a matter of some inconvenience to those interested in the preparation of scarlet fever products, but this inconvenience is mitigated by the realization that scarlet fever antitoxin would still be undiscovered unless the Dicks had used the method of skin tests in human beings for its study.

"Even before the use of scarlet fever antitoxin in the treatment of scarlet fever, the Dicks were able to show that antitoxin would probably be effective in the treatment of the disease. The fact that it neutralized scarlet fever toxin demonstrated this to some extent; but they showed further that the injection of a minute amount of antitoxin into the skin of a scarlet fever patient

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* Read before the Northern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, April 12, 1929, Cleveland, Ohio.

[1] Director, Biological Laboratories, E. R. Squibb & Sons, New Brunswick, N. J.

caused the disappearance of the rash at the site of injection. This is known as the blanching test, and it is useful in the diagnosis of doubtful cases of scarlet fever.

"Scarlet fever antitoxin is now available in a concentrated and purified form, comparable to the concentrated diphtheria and tetanus antitoxins. Its effect in scarlet fever can best be realized if I quote briefly from a recent paper by Dr. Edwin H. Place of the Harvard Medical School (*Jour. of the Medical Society of New Jersey*, Feb. 1929). 'After the injection of scarlet fever antitoxin the rash subsides with great rapidity, usually within 24–48 hours. It is often impossible to make a diagnosis 24 hours after antitoxin has been given. The throat symptoms, if unaccompanied by membrane and swelling, subside as rapidly. In surgical scarlet fever, the improvement is often miraculous; not only do the toxic symptoms subside rapidly but the severe advancing wound infection rapidly clears. Unfortunately, this does not always occur; but as a rule this group of infected wound cases, including the puerperal state, constitutes the most striking exhibit of the life-saving value of scarlet fever antitoxin.'"

"The Dicks also showed that the injection of a small amount of scarlet fever toxin into the skin of susceptible individuals caused the development of a red area. This is known as the Dick Test, and by its means we are enabled to detect individuals who are susceptible to scarlet fever. The Dicks further showed that susceptible individuals may be vaccinated against scarlet fever by the injection of increasing doses of scarlet fever toxin. Since prevention is better than cure, this prophylactic immunization against scarlet fever is perhaps to be regarded as their greatest discovery.

"The Dicks applied for a patent on their discoveries, which was granted in July 1925, in order that they might have control over the methods of production, dosage used and of standardization. The patent is administered by the Scarlet Fever Committee which has granted licenses to certain biological manufacturers for the production and sale of scarlet fever products under the control of that Committee. Products so produced have an additional control of their potency over that of the manufacturer and of the Government, which is an added guarantee that they are dispensed in the proper form and dosage, and may be relied upon to exert their full specific effect.

"Very soon after the discoveries of the Dicks, Dr. Birkhaug of the School of Medicine and Dentistry of the University of Rochester, Rochester, N. Y., announced that the streptococcus of erysipelas produced a toxin, and that a specific antitoxin could be prepared with this toxin. Erysipelas antitoxin is used extensively in the treatment of erysipelas, and is to be considered one of the outstanding discoveries of the past decade. According to Symmers and Lewis, who have had extensive clinical experience with erysipelas 'the antitoxin treatment of erysipelas marks an advance, the results of which are commensurate with those obtained in the treatment of diphtheria.' They state further that as far as the immediate attack is concerned, erysipelas is now a vanquished disease.

"Recent discoveries in regard to diphtheria have had to do almost entirely with the prevention of this disease. Von Behring, the discoverer of diphtheria antitoxin, first showed that the injection of a mixture of diphtheria toxin and diphtheria antitoxin produced immunity against the disease. This method was subsequently studied and standardized by Dr. William H. Park and his associates of the New York City Department of Health. The injection of three doses of toxin-antitoxin at weekly intervals has been repeatedly shown to immunize the individual against diphtheria.

"Diphtheria toxin-antitoxin is playing a larger and larger part in the prevention of diphtheria. The campaigns of education that have been carried on by the various health departments have been markedly effective, and parents now are generally acquainted with the fact that toxin-antitoxin is effective protection against diphtheria. Recently toxin-antitoxin has been still further improved by preparing it from concentrated antitoxin obtained from the sheep instead of the horse. This change was made because there is no possibility that sheep serum will sensitize the individual to subsequent injections of therapeutic serum from the horse, should these be necessary in later life.

"Another preparation called Toxoid is also used in the preventive immunization against diphtheria. Toxoid has been studied particularly by Dr. Ramon of the Pasteur Institute in Paris. Ramon found that if a small amount of formaldehyde is added to diphtheria toxin, the toxin lost its toxicity without destruction of its immunizing properties. Toxoid is used in the same manner as toxin-antitoxin. Toxoid has the advantage that it contains no foreign serum whatever.

It has been extensively used in France with the most satisfactory results. Many health officers in this country are now interested in determining whether toxoid is superior to toxin-antitoxin.

"It must be mentioned that manufacturers of biological products have made marked progress in the past 10 years in the concentration of antitoxins and serums. The progress here has been gradual and, for that reason, perhaps, has not been fully appreciated by the medical and pharmaceutical professions. This concentration has led to a much lower incidence of anaphylaxis and serum disease.

"Strange as it may seem to us now, it was at first supposed by many that these reactions of anaphylaxis were brought about by the antitoxin itself. It has been definitely shown, however, that the reactions are due to inert proteins present in all serum. The removal of a large part of these inert proteins during the process of concentration has resulted in a marked reduction in the incidence of these undesirable reactions and has given to modern physicians a degree of confidence in the safety and efficacy of antitoxins not possessed by physicians generally in the early days when only crude unconcentrated preparations were available.

"For some years prior to the World War, vaccination against typhoid fever had been required of all officers and men of our Army and Navy. Medical officers of both services were fully acquainted with its efficacy in preventing typhoid fever. It had not, however, attracted much attention as a means of preventing typhoid fever in civil life. During the past several years, however, an ever-increasing interest has been shown in typhoid vaccine by members of the medical profession in civil life. The army statistics of the World War have been most convincing in regard to the prophylactic value of typhoid vaccine. The layman, with his present keen interest in preventive medicine, frequently requests that his physician immunize him against typhoid fever, particularly whenever he may be exposed to infection, as on vacation trips. This popularization of typhoid vaccine is an advance of great potentialities in the saving of life and the prevention of sickness.

"Perhaps a few words should be said here about non-specific therapy. By this is meant the treatment of disease, not by a specific agent, but by some substance capable of producing a general reaction in the body in the hope that this reaction will aid in overcoming disease. Typhoid vaccine, milk, nucleic acid and a host of other substances have been tried with varying degrees of success in the treatment of diseases such as chronic arthritis. Possibly these methods of treatment are already beginning to pass into disuse. There remains, however, one outstanding success of non-specific therapy. I refer to the treatment of paresis with malaria. Paresis, as you know, is a late stage of syphilis, in which the cerebral cortex is attacked with the production of mental and physical abnormalities. Many of these patients led useless lives for a period of several years and always eventually died. Now these patients are artificially inoculated with malaria, another infection, and are allowed to pass through several febrile paroxysms. After this, the malarial infection is easily cured with quinine. Many paretics so treated are now leading active useful lives.

"The science of chemotherapy was founded by Paul Ehrlich. It was the aim of this new branch of knowledge to discover compounds with a selective toxic affinity for invading microorganisms and a relative low toxicity for the host. Everyone is acquainted with the brilliant researches which led to the introduction of arsphenamine in the treatment of syphilis, followed soon by neoarsphenamine. The most recent addition to the arsphenamines is sulpharsphenamine. This newer compound is especially suitable for the treatment of certain cases of syphilis, since it can be given intramuscularly in highly concentrated form. It also seems to be more uniform in its composition than neoarsphenamine, and more stable.

"In recent years much attention has been given to the chemotherapy of bacterial infections. This has resulted in the accumulation of a vast amount of useful information regarding certain antiseptics, particularly of dyes, such as gentian violet. Unfortunately, however, there has not been a single notable contribution in the chemotherapy of bacterial disease. It is doubtful to many workers whether any of the newer germicides have advantages even as a skin disinfectant over the time-honored tincture of iodine.

"In the closely related science of pharmacology, ephedrine is undoubtedly to be regarded as the outstanding achievement of recent years. The Chinese have used decoctions of a plant called mahuang in medicine for over 5000 years. Ephedrine, an alkaloid, is the active principle of this drug. It has an effect in the animal body very closely resembling that of epinephrine.

Its action is considerably slower, but it has the advantage that it can be taken by mouth and that the period of its physiological activity extends over a longer time. Ephedrine has proven of distinct value in the treatment of hay fever and asthma. We are indebted particularly to K. K. Chen for our knowledge of the pharmacology of ephedrine.

"In 1921 Maurice Hall discovered that carbon tetrachloride was efficacious in the treatment of hookworm disease. This valuable remedy now supplements thymol and oil of chenopodium in the treatment of this scourge of tropical and subtropical countries.

"In no field of medical research have the results been more brilliant or of greater value than in Endocrinology or the science of the internal secretions. We now have as many as 6 preparations from the organs or fluids of the animal body the value of which has been proved in conditions due to the lack of the essential principle, or hormone, of a gland of internal secretion.

"The first of these hormones was epinephrine from the suprarenal gland, the isolation of which in pure form was announced by Abel and Crawford in 1897. Since then we have had pituitary solution from the posterior lobe of the pituitary gland, thyroxin from the thyroid gland, insulin from the pancreas, parathyroid extract from that gland, and the female sex hormone which induces estrus.

"Thyroxin was obtained in pure form by Kendall in 1915, and found to have the same physiological properties as desiccated thyroid gland. It is possible by the use of thyroxin to employ more exact dosage and to avoid the variation in activity sometimes found in the desiccated thyroid. Further, it was determined by the intravenous administration of crystalline thyroxin that quantitative response within close limits could be obtained. In other words, the isolated hormone has the advantage of a pure principle over the crude material. Thyroxin is used for all those conditions due to a deficient secretion of the thyroid gland.

"All of you well know the hopeless outlook for a case of diabetes, particularly if under 20, before insulin first became available in 1923. It has been estimated that there are as many as 1,000,000 cases of diabetes in the United States, many of whom without insulin might expect an early death from diabetic coma. Insulin was discovered by Macleod, Banting, Best and Collip of the University of Toronto, and the patent granted them is administered by the Insulin Committee of that University. A limited number of licenses have been granted for the manufacture and sale of insulin under such control as will insure a product meeting their requirements. Some licensees have given much time to research for the development of improved methods for the preparation of insulin, so that the product as now available possesses many points of superiority over that first used. Especially have there been improvements in clarity, stability, uniformity and accuracy of standardization, freedom from reaction producing proteins and absence of pigmentary impurities.

"The last of the hormones to which reference will be made is the one variously designated as the female sex hormone, ovarian hormone and other names. The first preparations of this hormone were made from the entire ovary, but as a result of research in many laboratories it has been recovered from other parts of the female body and especially from certain fluids. In this respect the estrus-inducing hormone obtained from these various sources parallels insulin which may be obtained from organs or tissues other than the pancreas and which is identical in its physiological action when so obtained. The ovaries, in addition to being the reservoir for the ovum, also produce an internal secretion or hormone which is necessary for the proper functioning of the uterus and which also has effects upon metabolism and the nervous system. The lack of this hormone after puberty and until the menopause is well established is frequently attended with symptoms of a definite and often distressing nature. Various preparations of the ovary such as tablets, extracts, powder, have for years been used in the treatment of conditions attributed to ovarian hypofunction without, however, very definite results from their use. These preparations were not standardized and there were no tests available for quality or identity. Almost all were intended for oral administration.

"As a result of the work of investigators for the past 10 years, it has become possible to prepare a sterile aqueous solution of the estrus-inducing hormone, potent and physiologically standardized.

"American investigators have been prominent in the study of this hormone, among them being Allen, Doisy, Stockard, Pafanicolao, Long, Evans, Frank, Novak, Loeb, Pratt, Morrell and Powers.

"Doisy, Ralls and Jordan have outlined as the requirements of a satisfactory preparation of the estrus-inducing hormone the following:

1. That the hormone be dissolved in an innocuous, aqueous medium.
2. That it be assayed by the smear method.
3. That it be ampuled to contain 5 to 10 Rat Units per 1 cc.
4. That ample tests of its sterility and keeping qualities be made.
5. That it should have no effect upon the blood pressure of anesthetized dogs.

"A preparation meeting these conditions prepared from the amniotic fluid of cattle is now available under the name of Amniotin. In addition to its ability to induce estrus in spayed white rats it will also induce menstruation in spayed rhesus monkeys. Just as insulin, it is given by hypodermic injection. It is used in the various conditions associated with ovarian hypofunction and for palliating the symptoms of artificial or natural menopause.

"Mention should be made at this point of the discovery of Minot and Murphy of the value of liver and extracts of liver in the treatment of pernicious anemia. This discovery was a development of the work of Whipple and his associates. Previous to the use of liver the outlook for pernicious anemia was almost uniformly hopeless.

"This brief review of the advances in medicine and pharmacy would be very incomplete unless reference is made to the knowledge that has come to us in the past ten years of those mysterious principles or agents known as vitamines. Vitamines are substances which though present in minute quantities in foods are absolutely essential to the continuation of the life process. The deficiency diseases are the result of an insufficent amount of vitamines and are so named because of the lack of something in the diet. We are not able to say whether they exert their action as essential tissue components directly on the tissues or, as has been suggested by someone, through a hormone action. Possibly both of these views are correct. It appears that vitamine A is an essential factor in the normal chemical processes of all epithelial cells, and that vitamine D exerts a hormone action in mineral metabolism. They are chiefly produced as a result of the vital process of the lower forms of life, and have been grouped according to their solubility, that is, fat-soluble and water-soluble.

"Concerning these important principles, McCollum has stated that 'many continue to believe that common experience has shown the safety of allowing the appetite, financial means and custom to be the guide in the selection of food.' The discoveries of the existence of hitherto unknown food principles, and the biological assay of all of our more common food stuffs by approximately planned feeding experiments, have brought to light a number of specific kinds of malnutrition. These can be produced at will in animals; they are so strikingly like diseases which have long existed among human beings in certain places that they suggested the cause of the latter. The results of applying the knowledge of quality in foods to the study of human diseases has demonstrated that faulty diet has been and is the cause of much physical inferiority, illness and early mortality in infants and children: it has also been shown that careful attention to the food supply of the sick affords an effective means of cure in certain conditions and of relief and the extension of life in others."

There are five of these vitamines concerning which our knowledge of their source, action and use is definite. These vitamines are now designated as A, B, C, D and E, and each and all of them are essential to health.

Vitamine A is necessary to growth. Its absence is followed by a keritinization of the epithelial cells in all the tissues of the body. This keritinization is characterized by a change to a dry, chemically inactive type of cell which quickly falls prey to invading bacteria. It is found most abundantly in cod liver oil, butter fat, egg yolk, liver, leafy vegetables and yellow pigmented vegetables.

Vitamine B (the absence of which results in the development of beri-beri and also thought by Goldberger to be concerned in the cause of pellagra) contains two different principles—one known as the anti-neuritic factor and the other the p. p. factor. Vitamine B is most abundant in eggs and in cereals such as wheat and in yeast. A palatable form of vitamine B has been made from the germ of wheat. This preparation in addition to being a very concentrated form of vitamine B is of value in the modification of milk for infants on account of its dextrin-maltose content. Although very little beri is seen in the United States, recent researches in pediatrics have shown that infants in particular frequently suffer from vitamine B deficiency. This has

been recently emphasized by Hoobler (*J. A. M. A.*, 91 (Aug. 4, 1928), 307) who believes that a substance rich in vitamine B should be regularly prescribed for the infant dietary just as cod liver oil and orange juice are prescribed. This is particularly the case since neither human milk nor cow's milk are dependable sources of vitamine B.

"Vitamine C is the vitamine responsible for protection against scurvy, and is particularly abundant in orange juice and in certain fresh vegetables such as cabbage, carrots and tomatoes.

"Vitamine D is the anti-rachitic factor and controls the calcium-phosphorus metabolism of the body. In addition to its influence over growth, it is also effective in the proper development and growth of the teeth and bones. Its absence leads to the condition known as rickets. The most abundant source of the antirachitic factor or vitamine D is good cod liver oil. It is also found in butter, eggs and certain of the green vegetables. Curiously enough it has been found that the rays of the sun have the same action as this vitamine, also that the ultraviolet rays have this property which they can in turn transfer to certain other substances—thus conferring upon these substances an anti-rachitic action.

"In addition to the four vitamines just referred to there is also vitamine E which by some is thought to have an influence upon sterility and lactation.

"Our knowledge of the vitamines has increased the number of specific remedies in disease. Vitamine B, for instance, is a specific for beri-beri and certain types of marasmus in infants; vitamine C is a specific against scurvy, and vitamine D is a specific for rickets. The effect of vitamines in the treatment of these diseases is nothing short of spectacular. All four vitamines are probably concerned in resistance to infectious diseases. You can readily see, however, that the greatest good of our knowledge of vitamines will be accomplished by their prophylactic use. The coming generations will suffer much less from deficiency diseases than the present.

"This brief review of the developments in medicine and pharmacy of the last few years will serve the purpose of refreshing your knowledge of these developments and emphasizing that none of them have been made possible except as a result of patient research by workers in all parts of the world both in the laboratory and at the bedside. These developments in the prevention and treatment of disease have almost revolutionized the practice of medicine and pharmacy, yet nevertheless are probably to be regarded as the precursors of still more important progress in the immediate years of the future."

PROPOSED SURVEY OF THE DRUG TRADE.

Representatives of the industries and associations of the drug-trade activities met with representatives of the U. S. Department of Commerce to discuss a proposed survey of the drug trade, on January 20th. The meeting was called by Robert L. Lund, of St. Louis, for the purpose of discussing the desirability of petitioning the U. S. Department of Commerce to make a survey of the drug business, similar in import to the survey of the retail grocery business recently completed by the Department of Commerce in Louisville, Ky. It was the final decision of the group assembled that a petition should be presented to the Secretary of Commerce for such a survey and that the survey be made in and of the drug business of the City of St. Louis.

R. L. Lund was named Chairman of the meeting, and E. F. Kemp, secretary. Among those present from various organizations were:

From St. Louis, O. J. Cloughly, A. W. Pauley, R. L. Lund, Adolph C. Meyer, A. H. Grosse, W. H. Harper, Theo. F. Hagenow, H. C. Fink, John M. Drescher; Washington Wholesale Drug exchange, Paul Pearson and W. H. Bradbury; Federal Wholesale Druggists' Association, R. E. Lee Williamson, Baltimore; American Pharmaceutical Manufacturers' Association, H. Sheridan Baketel; AMERICAN PHARMACEUTICAL ASSOCIATION, E. F. Kelly, Secretary; Robert L. Swain and Samuel Hilton; National Association of Boards of Pharmacy, Augustus C. Taylor; Package Medicine Association, Roland Nutt; National Wholesale Druggists' Association, W. L. Crounse; National Association of Retail Druggists, Frank T. Stone; Proprietary Association of America, E. F. Kemp; Flavoring Extract Manufacturers Association, George M. Armor; and others; U. S. Department of Commerce, H. D. Cunn and T. L. Gaukel.

Secretary Lamont, Dr. Julius Klein and others of the Department were pleased with the movement and hopeful of success for such an undertaking. The survey necessitates a study of the many phases of the drug-trade activities, which need not be named—reflection will bring them to mind.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1929–1930.

Office of the Secretary, 10 West Chase Street, Baltimore, Md.

LETTER NO. 6.

January 9, 1930.

To the Members of the Council:

49. Committee on Unofficial Standards. Motion No. 13 (See Council Letter No. 5, page 83) has been carried and Mr. Gane has been advised.

No other nominations have been submitted in addition to that of Dr. Youngken, for the vacancy created by Mr. Gane's resignation.

(*Motion No. 17*) *It is moved by LaWall and seconded by Philip, that Dr. H. W. Youngken be elected a member of the Committee on Unofficial Formulas until 1932 to fill the unexpired term of Mr. E. H. Gane.*

50. Use of Text of N. F. V. Motion No. 14 (See Council Letter No. 5, page 83) has been carried and Messrs. Lea and Febiger have been advised.

51. Local Secretary for 1930 Meeting. No other nominations have been submitted in addition to that of Mr. S. Y. Harris, for Local Secretary.

(*Motion No. 18*) *It is moved by Dunning that Mr. S. Y. Harris be elected Local Secretary for the 1930 Meeting.*

52. Election of Members. Motions Nos. 15 and 16 (See Council Letter No. 5, pages 83 and 84) have been carried and applicants for membership numbered 91 to 111 inclusive and H-3 are declared elected.

53. Committee on Recipe Book. Mr. Thomas Roach, Oklahoma City, Okla., has been appointed by President Dunning, a member of this Committee until 1934 to fill the vacancy caused by the death of Mr. P. H. Utech.

54. Investment of Funds. Treasurer Holton advises that 5-$1000 City of Dallas, Texas, Bonds 4½%, due 1963, have been purchased for the Research Fund on a 4.40 basis.

55. Use of Text of N. F. V. The following communication has been received from Chairman DuMez of the Committee on Publications:

"I have examined the specimen pages of a textbook on Practical Pharmacy to be issued by Mr. Edward J. Smith, 1051 Manor Ave., Bronx, N. Y., and wish to recommend to the Council that Mr. Smith be granted permission to use the text of the N. F. V for partial reproduction to the extent indicated in these sample pages, under the usual conditions, and at the usual fee of $5.00.

"I also wish to recommend that P. Blakiston's Son & Co., Inc., be given permission to use the text of the N. F. V for partial reproduction in 'Properties and Uses of Drugs by Rusby, Bliss and Ballard,' under the usual conditions and at the usual charge of $5.00."

(*Motion No. 19*) *It is moved by DuMez that Edward J. Smith and P. Blakiston's Son & Co., Inc., be granted permission to use the text of the N. F. V for partial reproduction in a textbook on Practical Pharmacy and in Properties and Uses of Drugs by Rusby, Bliss and Ballard, respectively, and at the usual charge of $5.00 in each case.*

56. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 112, Charles F. Archer, 573 Talbot Ave., Dorchester, Mass.; No. 113, Abraham Chantz, 2138 Webster Ave., Pittsburgh, Pa.; No. 114, E. E. Duryee, Oxford, Nebr.; No. 115, Ed. J. Fleming, Blainesburg St., West Brownsville, Pa.; No. 116, Stephen Grayson, 1633 Leishman Ave., Arnold, Pa.; No. 117, Oscar L. Hancock, Manchester at Compton, Los Angeles, Cal.; No. 118, Harry T. Haefelin, 1420 Rush St., Philadelphia, Pa.; No. 119, Paul G. I. Lauffer, 245 E. 21st St., New York, N. Y.; No. 120, Robert Ellsworth Pattison, 1324 Liverpool St., Pittsburgh, Pa.; No. 121, Maurice M. Sclarsky, 1119 N. Euclid Ave., Pittsburgh, Pa.; No. 122, Alex Sieger, 1421 Beechview Ave., Pittsburgh, Pa.; No. 123, Clarence W. Sondern, 1425 Columbia Rd., N. W., Washington, D. C.; No. 124, Abraham Steinberg, 465 Hinsdale St., Brooklyn, N. Y.; No. 125, John Roland Stewart, 1809 West Street, Homestead, Pa.; No. 126, Y. C. Wong, 118 Michigan Ave., Detroit, Mich.

(*Motion No. 20*) *Vote on applications for active membership in the American Pharmaceutical Association.*

57. Applicants for Membership on Account of Contributions to the Headquarters Building Fund. The following non-members of the A. PH. A. have pledged $25.00 or more to the Headquarters Building Fund and have made a cash payment of $5.00 or more. They are entitled to membership and you are requested to vote on the applications which have been properly endorsed.

H-4, Lawrence H. Baldinger, Department of Pharmacy, University of Notre Dame, Notre Dame, Ind.; H-5, Isaac Cheskis, 6736 Glenwood Ave., Chicago, Ill.

(*Motion No. 21*) *Vote on applications of contributors to the Headquarters Building Fund for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

LETTER NO. 7.

February 12, 1930.

To the Members of the Council:

No. 58.—Committee on Unofficial Standards. Motion No. 17 (see Council Letter No. 6, preceding) has been carried and Dr. Youngken has been advised of his election.

No. 59.—Local Secretary for 1930 Meeting. Motion No. 18 (see Council Letter No. 6, preceding) has been carried and Mr. S. Y. Harris is elected Local Secretary. Mr. Harris invited the presidents and secretaries of the eight pharmaceutical associations of Maryland to form the Executive Committee in charge of arrangements for the meeting and they have accepted. The committee has organized, sub-committees have been appointed, and recommendations as to the Headquarters and as to the program for the meeting will be submitted to the Council later.

No. 60.—Use of Text of N. F. Motion No. 19 (see Council Letter No. 6, preceding) has been carried and Messrs. Edward J. Smith and P. Blakiston's Son & Co., Inc., have been so notified.

No. 61.—Election of Members. Motions Nos. 20 and 21 (see Council Letter No. 6, preceding) have been carried and applicants for membership numbered 112 to 126, inclusive, and H-4–5 are declared elected.

No. 62.—Life Membership. Messrs. J. Edison Good, New Cumberland, Pa., and E. F. Kelly, Baltimore, Md., have become Life Members of the A. PH. A. through the payment of $50 and $25, respectively.

No. 63.—Safe Deposit Boxes. Treasurer Holton desires to advise the Council that he has surrendered Box. No. 2 in the Baltimore Trust Company's vault and has taken Box No. 595, as a larger box is required. The President and Secretary are advising the Baltimore Trust Company that Treasurer Holton is to have access to and control over the contents of Box 595.

No. 64.—Letter from Dr. C. H. LaWall. Dr. LaWall writes in reference to the rising vote of thanks to him at the Rapid City meeting, for his contribution to pharmacy in the publication of "Four Thousand Years of Pharmacy:"

> "I cannot tell you how deeply I appreciate this generous spirit and through you I am thanking the officers and members of the ASSOCIATION who were present at that meeting."

No. 65.—Report of the Auditors. The following report has been submitted:

January 29, 1930.

Mr. C. W. Holton, Treasurer,
AMERICAN PHARMACEUTICAL ASSOCIATION,
Baltimore, Maryland.

Dear Sir:

I have made an examination of the books and accounts of the AMERICAN PHARMACEUTICAL ASSOCIATION and of your report as Treasurer, for the calendar year 1929, and I HEREBY CERTIFY that the total cash on hand at December 31, 1929, amounts to $370,017.89, which together with the cost of Real Estate in Washington, D. C., and Securities in your safe deposit box in the Baltimore Trust Company, total $593,571.22 as shown by your report.

I have also examined the records maintained by the Secretary of the ASSOCIATION and have traced the transfer of funds from his account to that of the Treasurer.

All cash receipts have been traced to deposits in bank to the credit of the respective funds for which received, and all disbursements have been found evidenced by properly authorized voucher checks.

Balances on deposit with the various banks have been reconciled with certificates from the depositories, and investment securities held by the ASSOCIATION have been examined and found to be in agreement with accounts shown by the records.

Respectfully submitted,
(Signed) W. A. JOHNSON,
Certified Public Accountant.

In order that the members of the Council and others interested may be informed, the following data is quoted from the Treasurer's Report for the year:

January 1, 1929 to December 31, 1929.

BALANCE AND RECEIPTS.

BALANCE.			
Cash in Merchants & Newark Trust Co., Newark, N. J.		$ 450.54	
Cash in Boston Penny Savings Bank		319.90	
Total balance January 1, 1929			$ 770.44
RECEIPTS.			
For the Current Fund.			
From the Secretary	$ 48,408.40		
Interest on deposit Boston Penny Savings Bank	16.16		
Interest on deposit Merchants and Newark Trust Co.	61.83		
Interest on Headquarters Building Fund	11,639.96	60,126.35	
For the Permanent Funds.			
Endowment	508.90		
Centennial	169.09		
Ebert Legacy	278.51		
Ebert Prize	45.08		
Life Membership	1,497.41		
Research	7,175.29		
Headquarters Building	105,985.54		
Headquarters Building (sale of bonds)	10,000.00	125,659.82	
For the Trust Funds.			
Wm. Procter, Jr., Monument	564.79		
J. P. Remington Honor Medal	31.34	596.13	
Total Receipts			$186,382.30
Total Balance and Receipts			$187,152.74

DISBURSEMENTS AND BALANCE.

From the Current Fund.	Budget appropriations.	Budget disbursements.
GENERAL EXPENSES.		
Salaries	$11,700.00	$11,699.92
Rent	1,020.00	1,020.00
Telegraph and Telephone	200.00	158.63
Clerical Expenses	1,500.00	1,486.00

Printing, Postage and Stationery		1,500.00	1,512.78
Office Supplies		150.00	122.48
Traveling Expenses		1,300.00	860.43
Premium on Bonds		60.00	50.00
Auditing		75.00	75.00
Certificates		50.00	62.50
Miscellaneous		150.00	121.39
Scientific Section		25.00	49.53
Section on Education and Legislation		25.00	31.84
Section on Practical Pharmacy and Dispensing		25.00	28.86
Section on Commercial Interests		25.00	22.93
Section on Historical Pharmacy		25.00	26.41
Commission on Proprietary Medicines		50.00	
Committee on Local Branches		25.00	
Committee on Membership		1,000.00	574.89
Committee on Legislation		100.00	
Committee on Syllabus		50.00	50.00
Committee on Unofficial Standards		50.00	64.25
Committee on Colored Glass Containers		50.00	
Drug Trade Bureau of Public Information		400.00	400.00
International Pharmaceutical Federation		120.00	
Metric Association		10.00	10.00
American Conference on Hospital Service		25.00	25.00
Headquarters Building Campaign		6,000.00	3,333.61
Year Book		4,500.00	3,693.36
Library		100.00	
Total Appropriation for General Expenses		$30,310.00	
Total Disbursements for General Expenses			$25,479.81
OPEN ACCOUNTS.			
JOURNAL		$11,000.00	$14,837.55
National Formulary		1,000.00	3,556.60
Recipe Book		1,000.00	9,838.65
Badges and Bars		50.00	
Amer. Joint Com. on Horticul. Nomen.		25.00	25.00
Total Budget Appropriations		$43,385.00	
Total Budget Disbursements			$53,737.61
Transfer of one-half net profits of National Formulary for 1928 to Research Fund			5,502.36
Total Disbursements from Current Fund by Voucher Check			$59,239.97
From the Permanent Funds.			
Endowment, Purchase of Bond	$ 1,017.58		
Centennial, Purchase of Bond	1,017.58		
Life Membership, Purchase of Bonds	2,995.26		
Research, Award for 1928–29	300.00		
Research, Award for 1929–30	750.00		
Research, Nat. Conference on Pharmaceutical Research	25.00		
Research, Expenses	28.20		
Research, Purchase of Bonds	18,308.85		
Headquarters Building, Transfer of Interest to Checking Account	11,639.96		

Headquarters Building, Taxes	557.64		
Headquarters, Building, Purchase of Bonds	189.74		
Total Disbursements from Permanent Funds by Voucher Checks		$ 36,829.81	
Total Net Credits to Permanent Funds		88,830.01	
Total Disbursements to Permanent Funds			$125,659.82
From the Trust Funds.			
Procter Monument, Purchase of Bond	1,000.53		
Remington Honor Medal, Purchase of Bond	1,029.35		
Remington Honor Medal, Medal for 1929	35.00		
Total Disbursements from Trust Funds by Voucher Check		2,064.88	
Less Amount withdrawn from Funds in Access of Receipts for the Year		1,468.75	
Total Disbursements to Trust Funds			596.13
Total Disbursements			$185,495.92

BALANCE IN CURRENT FUND.

Cash in Merchants and Newark Trust Co.	1,320.76	
Cash in Boston Penny Savings Bank	[illegible]6	
Total Balance in Current Fund, December 31, 1929		1,656.82
Total Disbursements and Balance		$187,152.74

COMPARISON OF FUNDS.

CURRENT FUND.

	Dec. 31, 1928.	Dec. 31, 1929
Cash in Merchants & Newark Trust Co.	$ 450.54	$ 1,320.76
Cash in Boston Penny Savings Bank	319.90	336.06
Total Current Fund	$ 770.44	$ 1,656.82

PERMANENT FUNDS.

Endowment Fund	$ 12,504.37	$ 12,995.69
Centennial Fund	4,824.23	4,975.74
Ebert Legacy Fund	7,087.00	7,365.51
Ebert Prize Fund	1,080.51	1,075.34
Life Membership Fund	36,067.04	37,569.19
Research Fund	48,674.19	54,300.89
Headquarters Building Fund	363,670.60	457,469.19
Total Permanent Funds	$473,907.94	$575,751.55

TRUST FUNDS.

Wm. Procter, Jr., Monument Fund	$ 14,283.53	$ 14,847.79
Jos. P. Remington Honor Medal Fund	1,348.07	1,315.06
Total Trust Funds	$ 15,631.60	$ 16,162.85

SUMMARY OF FUNDS.

Current Fund	$ 770.44	$ 1,656.82
Permanent Funds	473,907.94	575,751.55
Trust Funds	15,631.60	16,162.85
Total Funds	$490,309.98	$593,571.22

SUMMARY OF ASSETS AND TRUST FUNDS.

	Dec. 31, 1926.	Dec. 31, 1927.	Dec. 31, 1928.	Dec. 31, 1929.
Current Fund	$ 15,157.69	$ 4,119.65	$ 770.44	$ 1,656.82
Permanent Funds	310,869.35	369,565.88	473,907.94	575,751.55
Total Assets	$326,027.04	$373,685.53	$474,678.38	$577,408.37
Trust Funds	14,443.05	15,061.56	15,631.60	16,162.85
Total Funds	$340,470.09	$388,747.09	$490,309.98	$593,571.22

No. 66.—Delegates to U. S. P. Convention. President Dunning has appointed the following as delegates to the U. S. P. Convention in Washington, D. C., May 13th: J. H. Beal, Camp Walton, Fla.; S. L. Hilton, Washington, D. C.; E. F. Kelly, Baltimore, Md.

No. 67.—Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 127, Don Anthony, 10526 Hawthorne Blvd., Inglewood, Calif.; No. 128, Stanley M. Bahry, 5135 California St., Chicago, Ill.; No. 129, Norman H. Ballin, 3106 W. 16th St., Chicago, Ill.; No. 130, Harry Berlin, 1354 N. Artesian Ave., Chicago, Ill.; No. 131, Harry E. Bischoff, 118 48th St., Union City, N. J.; No. 132, Roland G. Boyce, 142 DeSota St., Pittsburgh, Pa.; No. 133, Chester M. Buckley, 106 Hall Avenue, Washington, Pa.; No. 134, Royal Carter, 926 Rogers St., Downers Grove, Ill.; No. 135, Ellen Cohen, 4147 Arthington St., Chicago, Ill.; No. 136, J. S. Colunga, 347 Convent St., Tucson, Ariz.; No. 137, John J. Debus, 396 Jackson Ave., Jersey City, N. J.; No. 138, Raymond A. Dobin, 1746 Roscoe St., Chicago, Ill.; No. 139, Henry V. Doyle, 21 Mile Square Road, Yonkers, N. Y.; No. 140, Albert Eaton, 121 W. Main St., Weatherford, Okla.; No. 141, William L. Edwards, 175 Pennsylvania Ave., East Liverpool, Ohio; No. 142, Loyal L. Foley, 94 S. George St., Chicago, Ill.; No. 143, Margaret C. Gallagher, 715 S. Wood St., Chicago, Ill.; No. 144, Rex Green, 1923 Geddes Ave., Ann Arbor, Mich.; No. 145, Henry Halz, 3001 Ganahl St., Los Angeles, Calif.; No. 146, Robert A. Hardt, c/o E. R. Squibb & Son, 111 N. Canal St., Chicago, Ill.; No. 147, Jon. J. Healy, Little Rock College, Little Rock, Ark.; No. 148, Adolph Katra, 2522 S. Clifton Pk. Ave., Chicago, Ill.; No. 149, Paul Kramer, 813 Locust Street, Pittsburgh, Pa.; No. 150, Philip A. Kustner, 1666 N. Vermont St., Los Angeles, Calif.; No. 151, A. J. Leudino, 1653 Sedgwick St., Chicago, Ill.; No. 152, Lucy M. Lewis, Librarian, Oregon State Agricultural College, Corvallis, Ore.; No. 153, Charles Bernard Marek, 3017 Montebello Ave., Baltimore, Md.; No. 154, Benjamin W. Menn, 3542 West Polk St., Chicago, Ill.; No. 155, August Jean Meola, 618 Larimer Ave., Pittsburgh, Pa.; No. 156, Edmond L. Merilh, 1029 Bourbon St., New Orleans, La.; No. 157, Rea P. Miller, Elizabeth, Pa.; No. 158, James L. Moore, 26 Marylea Ave., Brentwood, Pa.; No. 159, D. E. Murphy, 15354 Parkside, Detroit, Mich.; No. 160, Leighton C. Norris, 1906 Keyes Ave., Madison, Wis.; No. 161, Embree R. Rose, 42 Latham Court, Burlington, Vt.; No. 162, Robert Scott Ross, 217 1st St., Conemaugh, Pa.; No. 163, Luis M. Sanchez, 7a. del Fresno No. 294, Mexico City, Mex.; No. 164, George Frederick Schmitt, Jr., 1836 W. Mulberry St., Baltimore, Md.; No. 165, M. Lawrence Shields, 5821 Nicholson St., Pittsburgh, Pa.; No. 166, Harry Edward Speer, 812 E. 95th No. 4, Cleveland, Ohio; No. 167, Margaret C. Swisher, 3435 Main St., Buffalo, N. Y.; No. 168, Authur Louis Thomassy, 133 Fifth St., McDonald, Pa.; No. 169, Ernest H. Volwiler, c/o Abbott Laboratories, North Chicago, Ill.; No. 170, Carl A. Wulff, Box 34, Grafton, Wis.; No. 171, Boulos Zakhari, Abou Kerkas, Egypt.

(*Motion No. 22*) *Vote on applications for active membership in the American Pharmaceutical Association.*

No. 68.—Applicant for Membership on Account of Contribution to the Headquarters Building Fund. The following non-member of the A. PH. A. has pledged $25.00 or more to the Headquarters Building Fund and has made a cash payment of $5.00 or more. He is entitled to membership and you are requested to vote on the application which has been properly endorsed.

H-6, Manhall S. Wallner, 1117 13th St., Bedford, Ind.

(*Motion No. 23*) *Vote on applications of contributors to the Headquarters Building Fund for membership in the American Pharmaceutical Association.*

No. 69.—Committee on Transportation. Chairman Bradley announces that a reduced rate of one and one-half the regular fare has been secured for the Baltimore meeting and that the minimum number of certificates necessary to secure the reduced fare has been reduced to one hundred and fifty. Tickets will be good for return until May 17, 1930, which will take in the U. S. P. Convention in Washington, D. C., May 13th.

E. F. KELLY, *Secretary.*

COMMITTEES FOR BALTIMORE A. PH. A. MEETING.

Local Secretary Samuel Y. Harris has named the presidents and secretaries of Maryland and Baltimore pharmaceutical and drug organizations as chairmen of the various committees for the A. PH. A. meeting; they will select their associates; they are: Maryland Pharmaceutical Association—C. W. Colborn and C. C. Neal. Baltimore Retail Druggists' Association—W. G. Lauer and M. Strasburger. Drug Exchange Bureau—P. I. Heuisler and W. J. Lowry. Travelers' Auxiliary Maryland Pharmaceutical Association—C. C. Manchester and E. G. Helm. Alumni Association School of Pharmacy University of Maryland—A. Jackson and L. S. Williams. Baltimore Branch AMERICAN PHARMACEUTICAL ASSOCIATION—F. L. Black and B. Olive Cole. Maryland Board of Pharmacy—J. Fuller Frames and R. L. Swain. Baltimore Veteran Druggists' Association—W. M. Fouch and A. G. DuMez. AMERICAN PHARMACEUTICAL ASSOCIATION—President H. A. B. Dunning, Former President A. R. L. Dohme, Former President E. G. Eberle, Secretary E. F. Kelly. The committees named thus far are: Finance, P. I. Heuisler; Entertainment, W. G. Lauer, M. Strasburger, C. C. Manchester, E. G. Helm; Entertainment for Ladies, B. Olive Cole; Publicity, R. L. Swain; Program, C. C. Neal; Registration, F. L. Black; Hotels, S. Y. Harris; Veterans, W. M. Fouch; Alumni and Fraternities, Aquilla Jackson; Boards of Pharmacy, J. Fuller Frames; Schools of Pharmacy, A. G. DuMez; Visits to Industrial Plants, W. J. Lowry; Visits to Historial and Other Places of Interest, L. S. Williams.

THE WILLIAMSON BILL.

Dr. James H. Beal discussed the proposed transfer of prohibition enforcement to the Department of Justice (see JOUR. A. PH. A., 18 (1929), 1028) at the Rapid City meeting.

The Williamson bill (H. R. 8574) proposes the transfer of the Prohibition Bureau from the Treasury Department to the Department of Justice; it was bought up in the House under a special rule on February 6th.

It was stated during the consideration of the bill in the House that "the existing organization for enforcement of prohibition is an anomaly in that it divides the enforcement machinery. Detection of failure to comply with a chemical formula would better be left to the expert chemists and laboratories in the administrative division having to do with the issuance of permits for the use of medicinal and industrial alcohol, but detection of diversion, illegal stills, manufacture of alcoholic concoctions for beverage purposes, and possession, transportation or sale of intoxicants is quite beyond the purpose and scope of the Treasury department, which is primarily a fiscal agency.

"The Department of Justice should not be so loaded down with purely administrative matters that it will not be able to properly function as a law-enforcing agency. This is, and should remain, its primary function.

"In drafting the bill for the transfer of the enforcement division of the Bureau of Prohibition to the Department of Justice" Mr. Williamson said, "the Committee had endeavored to carry out these principles."

At the time of this writing no final action has been taken.

COMMITTEE REPORTS

REPORT OF THE COMMITTEE ON UNOFFICIAL STANDARDS.

The following portion of the report of the Committee on Unofficial Standards presents the tentative monographs for certain crude drugs and is published in the JOURNAL in order to afford opportunity for discussion before the standards proposed are finally adopted.

Manufacturers, importers, analysts and others interested in the proposed standards, are requested to send their criticisms and comments to the *Chairman of the Committee*, E. N. GATHERCOAL, 701 S. Wood St., Chicago.

ACHILLEA.

ACHILLEA.

Yarrow.—Milfoil.

Achillea consists of the dried flowering herb of *Achillea Millefolium* Linné (Fam. *Compositæ*).

Achillea contains not more than 2 per cent of harmless foreign organic matter and yields not more than 1 per cent of acid-insoluble ash.

Underground Achillea.—Stem furrowed and grayish hairy, branched at the top. Leaves up to 15 cm. long and 5 cm. broad, twice or thrice pinnatifid into linear divisions and more or less hairy. Inflorescence a dense, flat-topped corymb. Involucre cylindrical, 4 or 5 mm. long, its scales straw colored, rarely with dark margins, imbricated and keeled; receptacle flat and chaffy; the pistillate ray flowers 5 to 10, white or rarely crimson-tinged, 1.5 to 2.5 mm. long; the disk flowers yellow, perfect and fertile. Odor mildly aromatic. Taste mildly aromatic, bitter and astringent.

Powdered Achillea.—Light green or grayish green; leaf fragments, frequently the conical ends of the pinnæ terminating in a white point, with small-celled rather dense chlorenchyma, small spiral tracheæ and epidermis bearing hairs and rather narrowly oval stomata up to 0.040 mm. long; unicellular hairs numerous, colorless, shiny, mostly less than 0.020 mm. wide and up to 1.600 mm. long, or these hairs may be multicellular with 2 to 7 short uniseriate cells at the base and one very long terminal cell; glandular hairs few, yellowish brown, nearly globular, 1- or 2-celled, up to 0.050 mm. across; corolla fragments nearly colorless, lobes papillose, tubular base with short-stalked, colorless glands up to 0.075 mm. in diameter; pollen grains spheroidal, strongly spinose, up to 0.030 mm. across; involucral bract fragments with marginal cells elongated into papillæ or hairs and sometimes of a brown color and inner cells elongated, narrow, lignified, finely pitted; nearly colorless fragments of anther and of achene and rarely of yellowish brown papillose stigma; stem fragments with long hairs, lignified bast and tracheary tissue.

AGRIMONIA.

AGRIMONY.

Stickwort.

Agrimony consists of the dried flowering herb of *Agrimonia parviflora* Aiton (Fam. *Rosaceæ*).

Agrimony contains not more than 2 per cent of harmless foreign organic matter and yields not more than 1 per cent of acid-insoluble ash.

Unground Agrimony.—Stems up to 5 mm. in diameter, villous with brownish hairs. Leaves obovate or oblanceolate, imparipinnate, up to 15 cm. long and 9 cm. wide. Leaflets 9–17, spreading, lanceolate or linear-lanceolate, serrate, acuminate, glabrous above, pubescent beneath, very glandular, with 4 or 5 pairs of intermixed leaflets of small but variable sizes; stipules acuminate, lacinate. Flowers yellow, small, numerous, 6–10 mm. broad. Fruit turbinate, reflexed, small glandular, with an elevated disk and hooked prickles from erect to spreading. Odor faintly aromatic. Taste bitterish and astringent.

Powdered Agrimony.—Green or grayish green; thick-walled small-celled stem epidermis bearing hairs of three kinds, *viz.* (1) unicellular, smooth, thick-walled, lignified, brown-lumened

hairs frequently on multicellular pedestals and up to 3 mm. long and 0.050 mm. wide at the base; (2) unicellular, curved or wavy, pointed, verrucose, thick-walled, lignified hairs up to 0.300 mm. long and 0.015 mm. wide; (3) short multicellular hairs up to 0.075 mm. across, with a 1- or 2-celled stalk and 2- to 8-celled head; lignified bast masses with fibers up to 1 mm. long and 0.025 mm. wide associated with elongated, pitted parenchyma cells; masses of wood with pitted tracheids, wood fibers and wood parenchyma containing starch; masses of large, thin-walled pith parenchyma cells containing circular or angular starch grains, sometimes 2- or 3-compound and up to 0.025 mm. in diameter; leaf fragments with hairs like (2) described above, abundant on undersurface and along the leaf edge, small-celled chlorenchyma bearing many circular, yellowish, translucent secretion cells up to 0.060 mm. across and with the epidermis bearing broadly oval stomata up to 0.030 mm. long.

ANETHI FRUCTUS.

Dill Fruit.

Dill Fruit is the dried ripe fruit of *Anethum graveolens* Linné (Fam. *Umbelliferæ*).

Dill Fruit contains not more than 5 per cent of other fruits, seeds or other harmless foreign organic matter and yields not more than 0.5 per cent of acid-insoluble ash.

Unground Dill Fruit.—Cremocarps broadly oval, dorsally compressed, up to about 3 mm. in width and about 6 mm. in length; mericarps usually separated and free from a slender pedicel which may be up to 12 mm. in length; apex with a ring-like disk and two short projecting style remnants; externally brownish or greenish brown, each mericarp with three dorsal yellowish ridges and two broad lateral wing-like ridges. Odor and taste characteristic and aromatic.

Structure.—Mericarps somewhat pentagonal in transverse section; epidermis thin; mesocarp of tangentially elongated thin-walled cells bearing 6 oil-tubes, 2 on the commissural side and 1 on each of the lateral and dorsal sides, and a fibro-vascular bundle in each ridge, those in the 2 wing-like ridges much broadened, extending nearly to the outer edge of the wing; endodermis of tangentially elongated cells with thin, yellowish walls; a seed coat consisting of broad, brownish outer epidermal cells and several rows of collapsed cells; endosperm of polyhedral cells with somewhat thickened walls, the cells containing numerous oil globules, aleurone grains, and rosette aggregates of calcium oxalate either within the aleurone grains or free within the cells.

Powdered Dill Fruit.—Brownish; numerous irregular fragments of pericarp showing portions of oil-tubes from 0.090 to 0.260 mm. in width; fragments with tracheæ and fibers; cells of endosperm filled with aleurone grains, the latter up to 0.012 mm. in diameter and usually containing a rosette aggregate of calcium oxalate up to 0.006 mm. in diameter.

ANTHEMIS.

Anthemis.

English Chamomile.

Anthemis consists of the dried flower-heads of *Anthemis nobilis* Linné (Fam. *Compositæ*).

Anthemis contains not more than 2 per cent of harmless foreign organic matter and yields not more than 1 per cent of acid-insoluble ash.

Unground Anthemis.—Subglobular, 1.5 to 2 cm. in diameter; involucre hemispherical with two or three rows of nearly equal, elliptical, imbricated, pubescent bracts, having a yellow, scarious margin and a greenish middle portion; torus conical or convex, 3 to 4 mm. in height, solid or occasionally hollow; chaff scales similar to those of the involucre, about 2 mm. in length; ligulate corolla white or yellowish, 3-toothed, 4-nerved; ovary about 1 mm. in length, glandular, with a slender style and a 2-cleft stigma; tubular florets few or none, yellowish and perfect; achene oblong, with a pappus. Odor distinct; taste aromatic and bitter.

Powdered Anthemis.—Yellowish; numerous fragments of ligulate corollas, with epidermal cells modified into papillæ; fragments of involucral scales showing numerous long, unicellular, thin-walled, non-glandular hairs; pollen grains occasional, spheroidal, from 0.024 to 0.030 mm. in diameter; many long fibers from 0.006 to 0.012 mm. in width with strongly lignified walls; occasional rosette aggregates of calcium oxalate up to 0.010 mm. in diameter, from tissues of the achene or from basal portions of the ligulate florets.

ARNICÆ RADIX.

Arnica Root.

Arnica Root consists of the dried rhizome and roots of *Arnica montana* Linné (Fam. *Compositæ*).

Arnica Root contains not more than 5 per cent of leaves, stem bases, or other harmless foreign organic matter, and yields not more than 1 per cent of acid-insoluble ash.

Unground Arnica Root.—Rhizome cylindraceous, more or less curved or s-shaped, up to 10 cm. in length and 5 mm. in diameter; externally dark brown, with longitudinal or somewhat spiral furrows or at the upper portions with annular markings from leaf-scars, the upper surface having short stem-bases or stem-scars, the lower with numerous long coarse roots; fracture short. Roots brownish, numerous, curved, from 3 to 15 cm. in length and up to 1 mm. in diameter; longitudinally furrowed; fracture short and hard. Odor somewhat aromatic; taste aromatic and bitter.

Structure.—Rhizome.—An outer layer of several rows of brownish cork cells; a cortex of nearly isodiametric parenchyma cells, with numerous large resin-canals in the inner part, usually in pairs opposite the medullary rays; a distinct endodermis surrounding numerous collateral fibro-vascular bundles, separated by broad medullary rays; a pith of nearly spheroidal parenchyma with large intercellular spaces; in older rhizomes the pith may be partially or almost wholly hollow. Root.—Cork of a few layers of cells; cortex of isodiametric parenchyma cells with thick walls; resin-canals in an interrupted circle along the inner cortex; endodermis distinct, the cells with thickened inner and radial walls; a somewhat pentagonal, radial fibro-vascular bundle, with strongly lignified tracheæ and fibers.

Powdered Arnica Root.—Brownish gray; numerous fragments of cork showing rectangular or somewhat collapsed cork cells with brownish walls and usually a brownish amorphous content; fragments of cortical tissue of parenchyma cells associated with large resin canals; fragments of wood consisting of medullary ray cells, pith cells, strongly lignified wood fibers, or tracheæ with simple pores, or reticulate or spiral markings, the tracheæ from 0.012 to 0.045 mm. in diameter; irregular masses of inulin occurring either separately or within the parenchyma cells of pith, cortex or medullary ray. Portions of the powder when treated with Potassium Hydroxide, T.S. yield a golden-yellow solution.

CARTHAMUS.

CARTHAMUS.

Safflower.—American Saffron.

Carthamus consists of the dried tubular florets of *Carthamus tinctorius* Linné (Fam. *Compositæ*) from which the immature ovaries have been removed.

Carthamus contains not more than 1 per cent of harmless foreign organic matter and yields not more than 2 per cent of acid-insoluble ash.

Underground Carthamus.—Florets from orange-red to brownish red, and up to 2 cm. long, frequently broken or compressed; corolla tube deeply five-lobed, lobes 5 to 10 mm. long and 0.5 to 1.0 mm. broad; stamen tube of 5 united anthers, yellow, 4 to 7 mm. long and sometimes projecting beyond the corolla lobes; stigma club-shaped, yellowish brown, projecting about 2 mm. out of the anther tube; akenes absent in the commercial drug. Odor weak, characteristic. Taste somewhat bitter.

Powdered Carthamus.—Corolla fragments red, epidermis papillose near the apex of the lobe and with undulate walls near the edges of the lobe; vascular bundles of the corolla with spiral tracheæ and accompanied by secretion tubes containing a reddish brown, resinous substance; stamen fragments yellow and composed of elongated cells with very porous walls; pollen grains globular, ovoid or rounded-triangular, 0.035 to 0.070 mm. in diameter, finely papillose and frequently showing 3 excrescences.

Tests for Identity.—Mounted in ferric chloride solution, powdered carthamus markedly darkens to a deep brown hue. Heat one part of powdered carthamus in 50 parts of water to boiling, filter, and to 5 drops of the filtrate add 1 drop of ferric chloride T.S.; a dark brown coloration and precipitate is formed. Carthamus imparts a yellow color to water, ethyl alcohol, methyl alcohol and to solutions of sodium hydroxide, potassium hydroxide and ammonia; to

pyridine an orange-red color. Macerate 0.1 Gm. of powdered carthamus in 5 cc. of ammonia water, filter a few drops into a white dish and evaporate to dryness; a drop of concentrated sulphuric acid gives a dark red color with the yellow residue and a drop of ferric chloride T.S. a dark brownish color.

CHELONE.

CHELONE.

Balmony, Turtle Head.

Chelone consists of the dried leaves of *Chelone glabra* Linné (Fam. *Scrophulariaceæ*).

Chelone contains not more than 5 per cent of other parts of the plant, nor more than 2 per cent of harmless foreign organic matter and yields not more than 1 per cent of acid-insoluble ash.

Unground Chelone.—Leaves oblong-lanceolate, up to 15 cm. long and 8 cm. wide, smooth, with about 10 prominent veins on each side of the midrib, serrate with appressed teeth, acuminate; petiole short; turning nearly black in drying. Inodorous. Taste, bitter.

Powdered Chelone.—Blackish green; leaf fragments with palisade and spongy chlorenchyma and spiral tracheæ; epidermis from upper surface with angular, mostly 5-sided cells up to 0.085 mm. long and without stomata, and from lower surface with very sinuous lateral cell walls and numerous broadly oval stomata up to 0.030 mm. long; epidermis from lower surface of veins with elongated 4-sided cells and bearing occasional 2- to 4-celled, pointed trichomes up to 0.350 mm. long and with finely papillose cell walls; occasional woody stem fragments with spiral and reticulate tracheæ; a few rounded, nearly smooth pollen grains up to 0.040 mm. in diameter; rarely, fragments of the winged akenes with large air-filled cells with unlignified walls having barred markings or fragments of capsule with small fiber-like, lignified cells and unicellular trichomes.

EUPATORIUM PURPUREUM.

PURPLE EUPATORIUM.

Queen-of-the-Meadow, Joe-Pye Weed, Purple Boneset.

Purple Eupatorium consists of the dried leaves and flowering tops of *Eupatorium purpureum* Linné (Fam. *Compositæ*).

Purple Eupatorium contains not more than 2 per cent of harmless foreign organic matter and yields not more than 2 per cent of acid-insoluble ash.

Unground Purple Eupatorium.—Stems not over 4 mm. thick, purple, puberulent, usually hollow. Leaves oval to lanceolate up to 25 cm. long and 15 cm. wide, tapering base, acute or acuminate, toothed, glabrous above, scabrous-puberulent beneath with raised pinnate venation. Inflorescence, convex panicles on long spreading branches; heads purple, narrowly cylindrical, 5–8 flowered, bracts few, obtuse, corollas 3 to 5 mm. long, usually not exserted and achenes 3 to 4.5 mm. long, nearly black with a whitish pappus. Odor and taste faintly aromatic.

Powdered Purple Eupatorium.—Green or brownish green; numerous leaf fragments with chlorenchyma, spiral tracheæ and epidermis with broadly oval stomata up to 0.030 mm. long and glandular and non-glandular hairs; glandular hairs few, short, with 1- or 2-celled head up to 0.075 mm. across, with yellow contents; non-glandular hairs frequently curved, up to 0.9 mm. long, uniseriate, 3 to 10 cells, the terminal cell pointed; numerous fragments of white pappus bristles, many-celled, barbellate; occasional fragments of the papillose club-shaped stigma; pollen grains numerous, 0.025 to 0.035 mm. in diameter, spheroidal, spinose; stem fragments with collenchyma, bast with long, narrow, lignified fibers, and wood with dotted and scalariform tracheæ.

LACTUCA.

LETTUCE.

Wild Lettuce, Wild Opium.

Lettuce consists of the dried leaves and tops of *Lactuca Serriola* Linné, *Lactuca canadensis* Linné and *Lactuca spicata* (Lam.) Hitch. (Fam. *Compositæ*).

Lettuce contains not more than 2 per cent of other parts of the plant or other harmless foreign organic matter and yields not more than 2 per cent of acid-insoluble ash.

Unground Lettuce.—Stems flattened, furrowed, occasionally prickly, not over 4 mm. in diameter; leaves lanceolate, oblanceolate or oblong, up to 30 cm. long, glabrous, green or blackish, pinnatifid, sinuate or entire and in *L. Serriola* spinulose-denticulate; petiole and midrib broad and flattened and in *L. Serriola* spinose beneath. Infloresence in loose panicles; flowers pale yellow; achenes blackish, oval, flat, thin, capped by a filiform beak and with a white pappus. Odor, narcotic. Taste, bitter and acrid.

Powdered Lettuce.—Leaf fragments very thin with small round-celled chlorenchyma, spiral tracheæ and 3 or 4 layers of collenchymatous hypodermis at the margin; epidermis with oval stomata up to 0.030 mm. long on both upper and lower surface, trichomes absent; veins with bi-collateral bundles and a single row of latex cells 0.015 to 0.040 mm. across at the outer edge of both outer and inner phloem; spines on midrib up to 4 mm. in length, 0.500 mm. broad at base, multiseriate, the cells much elongated and somewhat lignified; marginal spines 0.160 to 1.500 mm. long and consisting of collenchyma covered by a papillose epidermis; occasional achene fragments, yellowish, with papillæ or club-shaped trichomes up to 0.150 mm. long; pappus hairs uni- or bi-serriate, each cell 0.050 to 0.075 mm. long, 0.005 to 0.008 mm. wide and ending in a very short projecting point.

PHYSOSTIGMA.

PHYSOSTIGMA.

Calabar Bean, Ordeal Bean.

Physostigma is the dried ripe seed of *Physostigma venenosum*, Balfour (Fam. *Leguminosæ*).

Physostigma yields not less than 0.15 per cent of the alkaloids of Physostigma, not more than 1 per cent of harmless foreign organic matter and not more than 0.5 per cent of acid-insoluble ash.

Unground Physostigma.—Oblong or ellipsoidal, reniform, somewhat compressed, from 15 to 36 mm. in length and from 10 to 15 mm. in thickness; externally reddish or chocolate-brown, smooth except near the brownish black groove where the surface is somewhat wrinkled, the groove being about 2 mm. in width and extending almost the entire length of the convex side and frequently bearing the remains of the whitish funiculus; the margin of the seed-coat on both sides of the groove somewhat elevated, thickened and of a yellowish or brownish red color; embryo large, white, with short hypocotyl and two concavo-convex cotyledons; taste at first starchy, afterwards acrid.

Structure.—A hard seed-coat consisting of an outer layer of palisade cells with non-lignified walls, much thickened on the outer and lateral sides except toward the inside ends where the side walls taper sharply, becoming very thin where they join the spongy layer beneath; a layer of 2 or 3 cells of spongy parenchyma, the cells triangular or branched, with somewhat thickened walls and a brownish amorphous content giving a black color with ferric chloride T.S.; a layer of 4 or 5 rows of tangentially elongated parenchyma with somewhat wavy, colorless walls; an endosperm layer of collapsed cells with bright yellow walls and with small spiral tracheæ running through it; cotyledons made up chiefly of nearly isodiametric parenchyma bearing starch and aleurone grains and surrounded by an epidermal layer of small cells. Along the groove a double layer of palisade cells the outer ones containing a blackish amorphous content, and a thicker spongy layer is found and directly at the base of the groove is a vascular bundle composed of tracheids with lignified reticulate thickenings.

Powdered Physostigma.—Grayish white; starch grains up to 0.150 mm. in diameter, numerous, ovoidal, ellipsoidal or reniform, usually with a distinct cleft and frequently with radiating or irregular fissures; fragments of seed-coat with very thick, reddish brown cells, being either palisade-like or irregular resembling stone cells; occasionally fragments showing tracheids with reticulate thickenings or very small spiral tracheæ. Excepting the walls of the tracheæ and tracheids, none of the tissue is lignified.

POLYGONUM.

POLYGONUM.

Smartweed, Waterpepper.

Polygonum consists of the dried herb of *Polygonum Hydropiper* Linné or of *P. acre* Humboldt, Bonpland and Kunth (Fam. *Polygonaceæ*).

Polygonum contains not more than 2 per cent of harmless foreign organic matter and yields not more than 2 per cent of acid-insoluble ash.

Unground Polygonum.—Stems up to 3 or 4 mm. thick, smooth, furrowed, nodes swollen, sheaths cylindrical, bristly fringed. Leaves lanceolate, up to 12 cm. long, acuminate, ciliate and like the calyx, pellucid-punctate. Flowers, greenish white or reddish, arranged in spikes which are erect or drooping, stamens 6 or 8 and styles 2- or 3-parted. Achenes black, dull or shining, minutely striate or smooth. Taste slightly acrid.

Powdered Polygonum.—Greenish brown or brown; leaf fragments numerous with brownish round-celled chlorenchyma, numerous globular secretion cells up to 0.060 mm. in diameter, occasional calcium oxalate rosettes up to 0.020 mm. in diameter and at the edge of the leaf, numerous appressed, multiserriate, non-glandular, pointed trichomes up to 1 mm. in length and 0.065 mm. wide at the base, with 4 to 10 narrow, thin-walled striated cells in each; leaf epidermis with broad oval stomata up to 0.030 mm. long, found on both surfaces of the leaf, and a striated cuticle on the lower surface; stem fragments with a heavy collenchymatous hypodermis, lignified bast and thin-walled wood fibers and dotted and spiral tracheæ up to 0.080 mm. in diameter; fragments of the stigma with sharp-pointed papillæ; achene fragments with a layer of small, angular, thick-walled, dark brown cells.

TANACETUM.

Tansy.

Double Tansy.

Tansy consists of the dried leaves and flowering tops of *Tanacetum vulgare* Linné (Fam. *Compositæ*).

Tansy contains not more than 5 per cent of stems over 3 mm. in diameter nor more than 2 per cent of harmless foreign organic matter and yields not more than 2 per cent of acid-insoluble ash.

Unground Tansy.—Stems nearly smooth, somewhat angled, inclined to purplish color. Leaves glabrous, short petiolate, pinnately dissected; ovate, oblong or obovate in general outline, up to 20 cm. long and 10 cm. wide; the pinnæ lanceolate or linear-oblong about 10 to 12 pairs, acute and pinnatifid, incised or crisped; midrib prominent and in European tansy both surfaces depressed-glandular and finely pellucid-punctate. Flower heads in terminal corymbs, yellow, up to 1 cm. across. Odor strongly aromatic. Taste slightly acrid and very bitter.

Powdered Tansy.—Green or dark green; leaf fragments, thin with spongy chlorenchyma, spiral tracheæ and epidermis cells on the lower surface with very sinuous and on the upper surface with nearly straight, delicate, lateral walls and on both surfaces broadly oval stomata up to 0.040 mm. long; hairs of four kinds, *viz.:* (1) non-glandular, uniseriate hairs up to 0.180 mm. long, with 4 to 10 rounded or somewhat oblong cells with yellowish brown contents; (2) non-glandular, unicellular, colorless hairs up to 0.500 mm. long, flattened, twisted and tangled; (3) glandular leaf hairs, 1- or 2-celled, globular to club-shaped, up to 0.120 mm. long, and which in European tansy are found in marked depressions and cause the pellucid-punctate appearance; (4) glandular achene hairs with short stalk and ellipsoidal head up to 0.085 mm. across. Fragments of involucral bracts with nearly transparent marginal cells and central portion with narrow, thick-walled libriform cells having numerous, simple pores; fragments of the yellow, tubular corolla with 5 short lobes and of the papillose, 2-parted stigma; pollen grains spheroidal, up to 0.030 mm. across and with fine spinose projections; nearly colorless achene fragments with attached yellowish glands.

NARCOTIC IMPORT QUOTAS CUT BY CONTROL BOARD.

The Federal Narcotics Control Board has announced its decisions regarding permits for the importation of crude opium and coca leaves for the calendar year 1930, involving a considerable reduction from the importations of last year.

WILLIAMSON BILL PASSED BY HOUSE.

The Willamson prohibition reorganization bill (H. R. 8574) transferring prohibition enforcement from the Treasury to the Department of Justice, was passed by the House, February 8th. The bill is now before the Senate.

EDITORIAL NOTES

Editor: E. G. EBERLE, 10 West Chase Street, Baltimore, Md.

Members of the Council, A. PH. A.: S. L. HILTON, *Chairman;* CHARLES H. LAWALL, *Vice-Chairman;* E. F. KELLY, *Secretary;* H. V. ARNY, A. G. DUMEZ, H. A. B. DUNNING, H. C. CHRISTENSEN, C. E. CASPARI, J. H. BEAL, W. BRUCE PHILIP, T. J. BRADLEY. *Ex-Officio Members:* D. F. JONES, *President;* A. L. I. WINNE, W. B. GOODYEAR, *Vice-Presidents;* C. W. HOLTON, *Treasurer;* E. G. EBERLE, *Editor of the Journal;* A. G. DUMEZ, *Editor of the Year Book;* R. L. SWAIN, *Chairman of the House of Delegates.*

Collaborators: The Members of the Council; E. FULLERTON COOK, *Chairman,* U. S. P. Revision Committee; E. N. GATHERCOAL, *Chairman,* N. F. Revision Committee; Chairmen of the Sections, A. PH. A.; H. A. LANGENHAN, GLENN L. JENKINS, H. C. NEWTON, DENNY BRANN, GEORGE D. BEAL; A. G. DUMEZ, *President,* A. A. C. P.; CHARLES B. JORDAN, *Chairman,* Executive Committee, A. A. C. P.; JOHN A. J. FUNK, *President,* N. A. B. P.; HENRY C. CHRISTENSEN, *Secretary,* N. A. B. P.

NEW AND NONOFFICIAL REMEDIES.

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

W. A. PUCKNER, *Secretary.*

VIOSTEROL.

Investigators working with various sterols discovered that ergosterol (originally derived from ergot but now obtained from other substances, mainly yeast), in crystalline form or in solution, when subjected to ultraviolet radiation develops an antirachitic (vitamin D) potency enormously greater than that of cod liver oil. For therapeutic use the ergosterol after irradiation is usually dissolved in a vegetable oil. The Council has adopted the term viosterol to designate irradiated ergosterol and viosterol in oil to designate a preparation containing this substance dissolved in oil. The Council has also provisionally adopted the qualifying phrases 100 D, 5 D, etc., to designate the vitamin D potency of the various preparations as multiples of the vitamin D potency of good cod liver oil. The potency of viosterol preparations is measured by the methods used for determining the vitamin D potency of cod liver oil.

Viosterol is for use in prophylaxis and treatment of rickets and, experimentally, in other conditions arising from faulty calcium and phosphorus assimilation. It should be borne in mind that viosterol does not contain vitamin A and that harm from hypercalcemia may result from the use of too large doses of the substance.

VIOSTEROL IN OIL 100 D.—Irradiated Ergosterol in Oil.—Activated Ergosterol in Oil.—Viosterol dissolved in a vegetable oil and standardized to contain 1333 rat units of vitamin D in each Gm., this strength being 100 times that of a potent cod liver oil used as a standard.

Actions and Uses.—See preceding article, Viosterol.

Dosage.—Daily prophylactic dose for the average infant and child, 8 to 10 drops (0.1233 to 0.1666 cc.: $2^2/_3$ to $3^1/_3$ minims); for the premature and rapidly growing infant, 15 drops (0.25 cc.: 5 minims); daily curative dose, 15 to 20 drops (0.25 to 0.333 cc.: 5 to 7 minims); in severe cases and for adults, doses in excess of 20 drops may be given. The marketed preparations are accompanied by a standard dropper designed to deliver 3 drops to the minim.

Viosterol in oil 100 D is standardized by comparison with a potent cod liver oil containing in each 0.75 mg. 1 rat unit of vitamin D, the rat unit being defined as that amount of vitamin D which, when uniformly distributed into the standard vitamin D deficient diet—ration 2965, *Jour. Biol. Chem.*, 64, 263 (1925)—will produce a narrow and continuous line of calcium deposits in the metaphyses of the distal ends of the radii and ulnae of standard rachitic rats.

Viosterol-Abbott.—A brand of viosterol in oil 100 D, N. N. R.

Manufactured by The Abbott Laboratories, North Chicago, under U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) by license of the Wisconsin Alumni Research Foundation.

Viosterol-Abbott is prepared by dissolving ergosterol in anhydrous, peroxide free ether-U. S. P.; the solution is filtered, placed in transparent quartz containers with reflex condensers, and exposed to ultraviolet rays at a determined distance and intensity for a determined length of time. The irradiated ergosterol, freed of ether and dissolved in maize oil, is biologically assayed and adjusted to have the potency of viosterol in oil 100 D, N. N. R.

Parke, Davis & Co.'s Viosterol.—A brand of viosterol in oil 100 D, N. N. R.

Manufactured by Parke, Davis & Co., Detroit, under U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) by license of the Wisconsin Alumni Research Foundation.

Parke, Davis & Co.'s Viosterol is prepared by dissolving ergosterol in warm alcohol; the solution is then irradiated by exposure to ultraviolet rays at a determined distance and intensity; after irradiation the solution is chilled and the crystalline ergosterol removed by filtration; the filtrate is dried under vacuum; it is then dissolved in maize oil and adjusted to have the potency of viosterol in oil 100 D, N. N. R.

Viosterol-Squibb.—A brand of viosterol in oil 100 D, N. N. R.

Manufactured by E. R. Squibb & Sons, New York, under U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) by license of the Wisconsin Alumni Research Foundation.

Viosterol-Squibb is prepared by dissolving ergosterol in ether; the solution is then irradiated by exposure to ultraviolet rays; after assay of the irradiated ergosterol for its antirachitic potency, it is dissolved in maize oil and adjusted to have the potency of viosterol in oil 100 D, N. N. R.

COD LIVER OIL WITH VIOSTEROL 5 D.—Viosterol dissolved in cod liver oil, the solution containing not less than 400 vitamin A units per Gm. when tested by the pharmacopeial method and 66.65 rat units of vitamin D per Gm., this antirachitic strength being 5 times that of a potent cod liver oil used as a standard.

Actions and Uses.—See preceding article, Viosterol. Cod liver oil with viosterol 5 D is proposed for use in conditions in which it is desired to supplement the administration of vitamin A with that of vitamin D.

Dosage.—For infants and young children, 2.5 to 3.3 cc. (53 to 67 minims) daily; for adults and in severe cases doses up to 7 cc. (140 minims) or more are given.

Cod liver oil with viosterol 5 D is prepared by addition of irradiated ergosterol to cod liver oil in such proportion that the finished product will contain not less than 400 vitamin A units per Gm. when tested by the pharmacopeial method, and 66.65 rat units of vitamin D per Gm., the rat unit being that amount of vitamin D which, when uniformly distributed into the standard vitamin D deficient diet—ration 2965, *Jour. Biol. Chem.*, 64, 623 (1925)—will produce a narrow and continuous line of calcium deposits in the metaphyses of the distal ends of the radii and ulnae of standard rachitic rats.

Abbott's Viosterol Cod Liver Oil.—A brand of cod liver oil with viosterol 5 D, N. N. R.

Manufactured by the Abbott Laboratories, North Chicago, under U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) by license of the Wisconsin Alumni Research Foundation.

Irradiated ergosterol, prepared by the method described under viosterol-Abbott, is added to cod liver oil and the finished product is required to have a vitamin A potency of not less than 500 pharmacopeial units and to have the vitamin D potency of cod liver oil with viosterol 5 D, N. N. R.

Squibb's Viosterol Cod Liver Oil 5 D.—A brand of cod liver oil with viosterol 5 D, N. N. R.

Manufactured by E. R. Squibb & Sons, New York, under U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) by license of the Wisconsin Alumni Research Foundation.

Irradiated ergosterol, prepared by the method described under viosterol-Squibb, is added to cod liver oil and the finished product is required to have a vitamin A potency of not less than 500 pharmacopeial units and to have the vitamin D potency of cod liver oil with viosterol 5 D, N. N. R.

Squibb's Viosterol Cod Liver Oil 5 D, Mint-Flavored.—A brand of cod liver oil with viosterol 5 D, N. N. R. containing 0.67 per cent of oil of spearmint as flavoring.

Manufactured by E. R. Squibb & Sons, New York, under U. S. patent 1,680,818 (Aug. 14, 1928; expires 1945) by license of the Wisconsin Alumni Research Foundation.

Irradiated ergosterol, prepared by the method described under viosterol-Squibb is added to cod liver oil containing 0.67 per cent of oil of spearmint as flavoring and the finished product is required to have a vitamin A potency of not less than 500 pharmacopeial units and to have the vitamin D potency of cod liver oil with viosterol 5 D, N. N. R.—*Jour. A. M. A.*, August 31, 1929.

SOME ASPECTS OF OPIUM ADDICTION.

In concluding an editorial on the above subject the *Journal of the A. M. A.* (February 1, 1930) comments: There is one encouraging outcome clearly manifested by the extensive studies of addicts. The addiction to morphine is not characterized by physical deterioration or impairment of physical fitness aside from the addiction *per se*. This may seem highly surprising. Yet detailed clinical examinations of many patients gave no evidence of change in the circulatory, heptatic, renal or endocrine functions.

Light remarks that when it is considered that the persons had been addicted for at least five years, some of them as long as twenty years, these negative observations are highly significant. Thus there are substantial grounds for the belief that, were it possible to relieve the addict of his addiction, complete rehabilitation might be expected. This makes the accomplishment of cure manifoldly desirable when the prospect of success leads to a healthy man rather than to a physiologic derelict.

According to Light, the abrupt withdrawal of morphine was accompanied by only slight changes in the physiologic mechanisms studied, changes that did not afford adequate explanation of the well-known and challenging withdrawal symptoms. The Philadelphia research, which warrants careful reading, indicates the necessity for a study of the addict from some new point of view in order to discover the factors which induce and maintain the state of addiction and which on abrupt withdrawal of the drug elicit the withdrawal symptoms.

BACTERIOLOGY SHOW.

The third annual bacteriological show was held at the University of Illinois, School of Pharmacy on January 22 and 23, 1930. The show consisted of work done during the semester, by senior students in Bacteriology. Other material shown consisted of all the available biological preparations and over one hundred marketed antiseptics and germicides, laboratory equipment, posters and charts.

Since the work in bacteriology laboratory includes the making of media, the twelve kinds as prepared by the students were shown, as well as the twenty-one kinds which are issued to the student for differentiation tests on the organisms studied.

Typical student culture preparations, of which about fifty are made, studied and reported on, besides reports and cultures of yeasts and molds, occupied a special table. Besides these cultures as prepared by students there was a well-lighted case with bacterial growths in giant tubes, each with a neatly labelled card explaining pathogenicity, habitat and some other characteristics.

A central display was the charted reports of the students on phenol coefficients of over seventy marketed antiseptics and germicides, each determination in duplicate.

Bacterial counts of some dozen different milk samples, air analysis of the school lecture halls, the nearby morgues and about thirty other interesting places in Chicago were displayed, each with a scientific interpretation by the student analyst. The presence of bacteria on common things was proved by exhibited cultures of over forty substances, some of which were: paper money, hair combings, handkerchiefs, finger nails, candy bars, door knobs, telephone receivers and mouthpieces, tooth brushes, fruit surfaces, street car straps, teeth tartar, the skin and others.

Among the equipment shown were autoclaves, hot air sterilizing ovens, Arnold sterilizers, equipment for the determination of hydrogen-ion concentration of media, bacteriological stains, dry ingredients of media and pencil tips. Several microscopes were set up and equipped with stained slides such as diphtheria, tuberculosis and typhoid germs. These were well lighted and fixed in focus so visitors to the show could view the bacteria as magnified 1200 x.

All exhibited material was neatly placarded in simple explanatory terms. Two well-versed attendants were at the exhibit to explain such items as the Wasserman test charts, serums, vaccines, antitoxins, a "mystery microscope," and others.

The show was well advertised in nearby student residences, schools and stores, by means of posters made by the students.

The show tables were set in a horse shoe pattern with one large central exhibit; this arrangement allowed easy access to the displays.

Over five hundred people visited the show during the two days it was open to the public. Many scientific people who visited the show expressed surprise and admiration at the scope of the student work. There was no admission charge.

PERSONAL AND NEWS ITEMS.

Lyman F. Kebler, long connected with the food and drugs activities of the Federal government in the agricultural and post office departments, has become medical director for the Tennessee Products Corporation, Nashville. The corporation, associated with the John McEntee Bowman health interests in connection with the Biltmore hotels, is installing in its new quarters in the Cummins station, Nashville, an extensive laboratory for research. Dr. Kebler was Chairman of the Section on Historical Pharmacy, last year.

Secretary Arthur G. Hulett writes of the activities of Arizona Association in behalf of the Pharmacy Corps Bill and State matters. The State Association will meet in Prescott.

Dean Ernest Little, of New Jersey College of Pharmacy, was host, on January 13th, to a committee of pharmacists who met to discuss public education regarding services rendered by pharmacists in their respective neighborhoods. The Board of Trustees of Rutgers University has authorized the erection of a $60,000 addition to the College of Pharmacy Building.

Dean A. G. DuMez, University of Maryland, School of Pharmacy, advises that the removal of the school to its new building has been completed. Many large and important additions have recently been made to the library.

The former *American Registered Pharmacist* journal is now *The American Pharmacist.* Under a new name the publication has been enlarged and its purpose to promote professional pharmacy will be strengthened accordingly.

Dr. Oliver Kamm, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, has been elected President of the Michigan Academy of Science, Arts and Letters.

Prof. Anton Hogstad, Jr., has been named pharmacognosist to Missouri Botanical Gardens. Through an arrangement with the Missouri Botanical Gardens a Medicinal Plant Garden was established as a coöperative project by the former and the St. Louis College of Pharmacy. The botanical work with medicinal plants will be largely extended under the direction of Professor Hogstad who is especially interested in the origin, nature and physiological rôle of drug plant constituents.

Edward S. Sater, formerly engaged in A. PH. A. publicity work and in promoting Headquarters project is now associated with the Lambert Pharmacal Co. He will maintain headquarters at Minneapolis from where he will look after the interests of the company in five of the western states.

Secretary J. G. Beard of the North Carolina Pharmaceutical Association is endeavoring to complete the biographical sketches of the officers of North Carolina Pharmaceutical Association. Only a few more are needed to complete the files.

B. M. Keene, member of the Executive Committee of the N. A. R. D., was guest of honor at a luncheon on January 15th; retail druggists and other friends were host for this occasion. Secretary S. C. Henry and Chairman Julius Riemenschneider were among the out-of-town visitors. Mr. Keene is a former secretary and chairman of the Section on Commercial Interests, A. PH. A.

WEST VIRGINIA BULLETIN.

The *West Virginia Bulletin C-5* interestingly discusses the condition of pharmacy and continues its coöperative messages in behalf of the Pharmacy Corps and Capper-Kelly Bills.

OBITUARY.

EDWARD F. WAGENER.

Prof. E. F. Wagener, member of the AMERICAN PHARMACEUTICAL ASSOCIATION and of the faculty of the Indianapolis College of Pharmacy, died at the St. Francis Hospital, Indianapolis, on January 14th, after a short illness. Professor Wagener was 45 years of age. He was born in Indianapolis and received his education there, being a member of the first graduating class of the Indianapolis College of Pharmacy, in 1905. One year later he received his degree of pharmaceutical chemist. He conducted a drug store in his home city, served as secretary of the local draft board during the war and joined the teaching staff of the Indianapolis College in 1919. He was a member of the Indiana Pharmaceutical Association, the Masonic fraternity and other organizations.

Professor Wagener was unmarried. A sister and two brothers survive.

EDWARD PRESTON HOLLOWAY.

E. P. Holloway, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, and formerly of the Franz, Holloway Drug Co., of Denver, died December 21st, aged 71 years. The store with which the deceased was associated for quite a number of years was disposed of several months ago, and Mr. Holloway retired on account of impaired health.

Before coming to Colorado, Mr. Holloway had been engaged in the drug business at Kansas City. He was associated with Trunk Brothers in Denver for many years and manager of one of their branch stores which he purchased in 1916.

Mr. Holloway was a widower and is survived by an aunt, Mrs. Sadie S. Franz and a niece, Miss Eleanor Ruth Owens. He was highly regarded by his associates and patrons.

SOCIETIES AND COLLEGES.

ABSTRACTS OF PAPERS.

Abstracts, preferably not over 100 words, should accompany all titles of papers when sent to the secretaries of the various A. PH. A. Sections. The officers ask contributors to send in their papers and abstracts in order to facilitate proper coöperation and enable the secretaries to have mimeographed copies of abstracts ready in advance of the meeting. Papers should reach the officers in time for action that may be necessary for giving them place on the program.

SECTION OFFICERS.

So that contributors of papers may have the addresses of the chairmen and secretaries before them, they are given here; a complete list of officers will be found on page X of the Advertising Section.

Scientific Section.—*Chairman*, H. A. Langenhan, % U. of Washington, Seattle, Wash.; *First Vice-Chairman*, E. E. Swanson, Indianapolis, Ind.; *Second Vice-Chairman*, W. J. Husa, Gainesville, Fla.; *Secretary*, L. W. Rowe, % Parke, Davis & Co., Detroit, Mich.

Section on Education and Legislation.—*Chairman*, Glenn L. Jenkins, Lombard and Greene Sts., Baltimore, Md.; *Vice-Chairman*, B. V. Christensen, Gainesville, Fla.; *Secretary* Rudolph H Raabe, Ada, Ohio.

Section on Practical Pharmacy and Dispensing.—*Chairman*, H. C. Newton, Omaha, Neb.; *Vice-Chairman*, Charles V. Netz, Minneapolis, Minn.; *Secretary*, E. O. Leonard, Pocatello, Idaho.

Section on Commercial Interests.—*Chairman*, Denny B[illegible] Moines, Ia.; *Vice-Chairman*, Jos. [illegible]h, Omaha, Neb.; *Secretary*, Rowland [illegible], Gettysburg, So. Dak.

Section on Historical Pharmacy.—*Chairman*, George D. Beal, University of Pittsburgh, Pittsburgh, Pa.; *Secretary*, J. T. Lloyd, Court and Plum Sts., Cincinnati, O; *Historian*, E. G. Eberle, 10 W. Chase St., Baltimore, Md.

NATIONAL ASSOCIATION OF RETAIL DRUGGISTS TO MEET IN ATLANTIC CITY.

For the second time in its history, the National Association of Retail Druggists will hold its annual convention in Atlantic City, N. J., during the week of September 15th.

The Atlantic City invitation was presented in person by President Dudley G. Singer, of the New Jersey Pharmaceutical Association. Mr. Singer has been appointed Executive Director of the convention and Secretary Prescott R. Loveland, of the New Jersey Pharmaceutical Association, has been named Executive Secretary.

The tenth annual meeting of the N. A. R. D. was held at Atlantic City in 1908.

VIRGINIA LEGISLATION.

Secretary A. L. I. Winne is reporting the status of Virginia legislation by means of bulletins. House Bill No. 8 seeks to do away with "Assistant Pharmacist" examinations; it has passed the House and is now with the Senate. Senate Bill No. 104 seeks to restrict jury duty exemption to one individual of each pharmacy. Senate Bill No. 182 provides a stamp tax on alcohol-containing medicinals, including also "canned heat" and kindred products—the tax is objectionable and excessive. A bill seeks to place additional tax on chain stores. Another bill restricts the sale of barbital and kindred preparations to physicians' prescriptions.

PROPRIETARY ASSOCIATION WILL MEET IN CANADA.

Windsor Hotel, Montreal, Canada, has been selected as the place of meeting for the Proprietary Association's annual convention. The meeting will start on Tuesday, May 20th, and will continue for three days. An invitation has been extended to the Proprietary Association of Canada to meet jointly with the American Association.

THE NATIONAL PHARMACEUTICAL ASSOCIATION OF CUBA CELEBRATES.

On February 24th the National Pharmaceutical Association will hold a meeting honoring its President—Miguel Fernandez Garrido, and its Secretary—José Capote Diaz. An invitation to attend has been received and fraternal greetings and good wishes were extended.

IOWA PHARMACEUTICAL ASSOCIATION.

Iowa Pharmaceutical Association held its annual meeting in Des Moines February 18th–21st. Among the speakers on the program were Walter H. Cousins, Elmer U. Berdahl, Douglas Malloch, George Judisch, Clyde L. Eddy and A. J. Dunlap.

KENTUCKY SEEKS TO RESTRICT USE OF NAME—DRUG STORE, ETC.

Legislation is sought by Kentucky pharmacists to restrict the designation of a drug store pharmacy or apothecary to the general application and the further requirement that a registered pharmacist shall constantly be in charge of establishment.

OHIO STATE PHARMACEUTICAL ASSOCIATION.

The annual meeting of the Ohio State Pharmaceutical Association will be held on board the steamer Juniata, June 15th–19th. Members and those who intend to be present during the annual meeting are asked to make reservation as early as possible so that the final arrangements can be made for chartering the steamer. The total expense of the trip will approximate $30.00 per passenger. All communications should be addressed to Secretary Theodore D. Wetterstroem.

ANNUAL MEETING OF THE BALTIMORE RETAIL DRUGGISTS' ASSOCIATION.

The annual meeting of the Baltimore Retail Druggists' Association was held at the Lord Baltimore Hotel, January 13th, Samuel Y. Harris, presiding. The officers' reports were followed by an address by District Attorney Herbert R. O'Connor.

L. M. Kantner as Chairman of the Committee on Nominations announced the following nominees for officers of 1930: *President*, Samuel Y. Harris; *Secretary*, M. Strasburger; *Treasurer*, P. J. Boenning; *First Vice-President*, W. G. Lauer; *Second Vice-President*, L. S. Williams; *Third Vice-President*, George P. Grau; *Fourth Vice-President*, A. F. Ludwig; *Recording Secretary*, W. H. Kratz. The nominees were elected.

President Harris appointed the committees for the ensuing year; he also announced March 6th as the tentative date of the annual banquet.

NEW YORK RETAIL DRUGGISTS' ASSOCIATION.

The following officers were elected for the ensuing year at the annual meeting of the New York Retail Druggists' Association: *President*, Harry Goldschmidt; *Vice-Presidents*, Max Canter, S. A. Goldstein and A. Kaufman; *Financial Secretary*, Ben Robbins; *Recording Secretary*, Morris Stieglitz; *Corresponding Secretary*, Nathaniel Levy; *Treasurer*, Barnet Miller.

S. A. Goldstein and Meyer A. Feinberg were chosen delegates to the United States Pharmacopœial convention. The thirty-third annual banquet of the organization was held at Hotel Commodore on January 26th.

RHO CHI ESTABLISHES CHAPTER AT UNIVERSITY OF NORTH CAROLINA.

Chapter XI of Rho Chi was established at the University of North Carolina on December 7th. The installation ceremonies took place in the Pharmacy Building, under the supervision of Dean L. S. Blake, of the School of Pharmacy at the Alabama Polytechnic Institute at Auburn. A banquet was tendered Dean Blake at the Carolina Inn by the charter members—Messrs. D. B. Browning, Rocky Mount; D. F. Chamblee, Richmond, Va.; J. T. Dillehay, Southern Pines; F. W. Dayvault, Mooresville; W. C. Barnwell, Reidsville; T. A. Libbus, New Bern and H. E. Bolen, Schoolfield, Va. Prof. J. G. Beard was made an honorary member.

LEGAL AND LEGISLATIVE.

COÖRDINATION OF THE PUBLIC HEALTH ACTIVITIES.

The Committees of the Senate and House to whom S. 3167 and H. R. 8807 were referred have reported favorably on the Bill which follows. Support has been given the Bill by pharmacists; it is known as the Parker Bill, to which reference has heretofore been made.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That upon the request of the head of an executive department or an independent establishment which is carrying on a public-health activity the Secretary of the Treasury is authorized to detail officers or employees of the Public Health Service to such department or independent establishment in order to coöperate in such work. When officers or employees are so detailed their salaries and allowances shall be paid by the Public Health Service from applicable appropriations.

SEC. 2. (*a*) The Surgeon General of the Public Health Service is authorized to detail personnel of the Public Health Service to educational and research institutions for special studies of scientific problems relating to public health and for the dissemination of information relating to public health, and to extend the facilities of the Public Health Service to health officials and scientists engaged in special study.

(*b*) The Secretary of the Treasury is authorized to establish such additional divisions in the Hygienic Laboratory in the District of Columbia as he deems necessary to provide agencies for the solution of public-health problems, and facilities therein for the coördination of research by public-health officials and other scientists and for demonstrations of sanitary methods and appliances.

SEC. 3. The administrative office and bureau divisions of the Public Health Service in the District of Columbia shall be administered

as a part of the departmental organization, and the scientific offices and research laboratories of the Public Health Service (whether or not in the District of Columbia) shall be administered as a part of the field service.

SEC. 4. Hereafter, under such regulations as the President may prescribe, medical, dental sanitary engineer, and pharmacist officers selected for general service in the regular corps of the Public Health Service and subject to change of station shall be appointed by the President, by and with the advice and consent of the Senate; original appointments shall be made only in the grade corresponding to that of assistant surgeon or passed assistant surgeon, except as provided under Sections 5 and 6 of this Act.

SEC. 5. The President is authorized to appoint, by and with the advice and consent of the Senate, to grades in the regular corps not above that of medical director, under such regulations as he may prescribe, not to exceed a total of fifty-five medical, dental, sanitary engineer and pharmacist officers in the Public Health Service upon the date of passage of this Act (except commissioned officers of the regular corps). Not more than four such appointments shall be in a grade above that of surgeon. In making such appointments due regard shall be had to the salary received by such officer at the time of such appointment. For purposes of pay and pay period, said officers shall be credited only with active service in the Public Health Service and active commissioned service in the Army and the Navy.

SEC. 6. The Secretary of the Treasury is authorized to order officers in the reserve of the Public Health Service to active duty for the purpose of training and of determining their fitness for appointment in the regular corps and such active duty shall be credited for purposes of future promotion in the regular corps.

SEC. 7. Whenever commissioned officers of the Public Health Service are not available for the performance of permanent duties requiring highly specialized training and experience in scientific research, the Secretary of the Treasury shall report that fact to the President with his recommendations, and the President, under the provision of this section, is authorized to appoint, by and with the advice and consent of the Senate, not to exceed three persons in any one fiscal year to grades in the regular corps of the Public Health Service above that of assistant surgeon, but not to a grade above that of medical director; and for purposes of pay and pay period any person appointed under the provisions of this section shall be considered as having had on the date of appointment service equal to that of the junior officer of the grade to which appointed.

SEC. 8. Any person commissioned in the regular corps of the Public Health Service under the provisions of this Act of an age greater than forty-five years, if placed on waiting orders for disability incurred in line of duty, shall receive pay at the rate of 4 per centum of active pay for each complete year of service in the Army, Navy or Public Health Service, the total to be not more than 75 per centum.

SEC. 9. Hereafter commissioned officers of the regular corps of the Public Health Service, after examination under regulations approved by the President, shall be promoted according to the same length of service and shall receive the same pay and allowances as are now or may hereafter be authorized for officers of corresponding grades of the Medical Corps of the Army, except that—

(*a*) For purpose of future promotion an officer whose original appointment to the regular corps under the provisions of this Act is in a grade above that of assistant surgeon shall be considered as having had on the date of appointment service equal to that of the junior officer of the grade to which appointed; if the actual service of such officer in the Public Health Service exceeds that of the junior officer of the grade, such actual service not exceeding ten years for a passed assistant surgeon, and fourteen years for a surgeon shall be credited for purposes of future promotion;

(*b*) Pharmacists shall not be promoted to the grade of passed assistant surgeon until after five years of service in the grade of assistant surgeon and shall not be promoted above the grade of passed assistant surgeon.

(*c*) When an officer, after examination under regulations approved by the President, is found not qualified for promotion for reasons other than physical disability incurred in line of duty—

(1) If in the grade of assistant surgeon, he shall be separated from the service and paid six months' pay and allowances;

(2) If in the grade of passed assistant surgeon, he shall be separated from the service and paid one year's pay and allowances; and

(3) If in the grade of surgeon or of senior surgeon, he shall be reported as not in line of promotion, or placed on waiting orders and paid at the rate of $2^1/_2$ per centum for each

complete year of active commissioned service in the Public Health Service, but in no case to exceed 60 per centum of his active pay at the time he is placed on waiting orders.

SEC. 10. (*a*) The President is authorized to prescribe appropriate titles for commissioned officers of the Public Health Service other than medical officers, corresponding to the grades of medical officers. Hereafter officers of the Public Health Service in the grade of Assistant Surgeon General (except those in charge of bureau divisions) shall be known and designated as medical directors. The limitation now imposed by law upon the number of senior surgeons and Assistant Surgeons General at large of the Public Health Service on active duty is hereby repealed. There is created in the regular corps of the Public Health Service the grade of senior medical director, and the salary and allowances of officers commissioned in said grade, of whom there shall be two in number on active duty, shall be the same as that authorized in Section 8 of the Act approved June 10, 1922, for the Surgeon General of the Public Health Service.

(*b*) Hereafter the Surgeon General of the Public Health Service shall be entitled to the same pay and allowances as the Surgeon General of the Army; and a regular commissioned officer of the Public Health Service who serves as Surgeon General shall, upon the expiration of his commission, if not reappointed as Surgeon General, revert to the grade and number in the regular corps that he would have occupied had he not served as Surgeon General.

(*c*) The officer detailed as chief of the narcotics division of the Public Health Service shall, while thus serving, be an Assistant Surgeon General, subject to the provisions of law applicable to Assistant Surgeons General in charge of other administrative divisions of the Public Health Service.

SEC. 11. Hereafter the Secretary of the Treasury shall appoint, in accordance with the civil service laws, all officers and employees, other than commissioned officers, of the Public Health Service, and may make any such appointment effective as of the date on which the officer or employee enters upon duty.

SEC. 12. Hereafter officers of the Public Health Service when disabled on account of sickness or injury incurred in line of duty shall be entitled to medical, surgical and hospital services and supplies under such regulations as the Secretary of the Treasury may prescribe.

SEC. 13. Hereafter the advisory board for the Hygienic Laboratory shall be known as the National Advisory Health Council, and the Surgeon General of the Public Health Service, with the approval of the Secretary of the Treasury, is authorized to appoint, from representatives of the public-health profession, five additional members of such council. The terms of service, compensation, and allowances of such additional members shall be the same as the other members of such council not in the regular employment of the Government, except that the terms of service of the members first appointed shall be so arranged that the terms of not more than two members shall expire each year. Such council, in addition to its other function, shall advise the Surgeon General of the Public Health Service in respect of public-health activities.

CAPPER-KELLY FAIR TRADE BILL NEARING ENACTMENT.

The Committee on Interstate and Foreign Commerce of the House, through Mr. Merritt on January 27th, reported and recommended to passage of H. R. 11, as amended; it provides as follows:

That no contract relating to the sale of a commodity which bears (or the label or container of which bears) the trade-mark, brand or trade name of the producer of such commodity, and which is in fair and open competition with commodities of the same general class produced by others, shall be deemed to be unlawful, as against the public policy of the United States, or in restraint of interstate or foreign commerce, or in violation of any statute of the United States, by reason of any agreement contained in such contract—

That the vendee will not resell such commodity except at the price stipulated by the vendor.

SEC. 2. Any such agreement in a contract in respect to interstate or foreign commerce in any such commodity shall be deemed to contain the implied condition—

(*a*) That during the life of such agreement all purchasers from the vendor for resale at retail in the same city or town where the vendee is to resell the commodity shall be granted equal terms as to purchase and resale prices;

(*b*) That such commodity may be resold without reference to such agreement—

(1) In closing out the owner's stock for the purpose of discontinuing dealing in such commodity or of disposing, toward the end of a

season, of a surplus stock of goods specially adapted to that season;

(2) With notice to the public that such commodity is damaged or deteriorated in quality, if such is the case; or

(3) By a receiver, trustee or other officer acting under the orders of any court, or any assignee for the benefit of creditors.

SEC. 3. Nothing contained in this act shall be construed as legalizing any contract or agreement between producers or between wholesalers or between retailers as to sale or resale prices.

SEC. 4. As used in this act—

(1) The term "producer" means grower, packer, maker, manufacturer or publisher.

(2) The term "commodity" means any subject of commerce.

In discussing the provisions of the bill, Mr. Merritt stated that substantially what is accomplished by the bill "is to restate the principle of the common law and to restore liberty of contract so far as the Sherman Act interferes with that liberty in the special class of cases covered by the bill." We are quoting from Mr. Merritt's remarks in the following statements. "It is perfectly obvious that if any dealer sells part of his stock at or below cost he must, in order to keep in business, sell other portions of his stock at a profit higher than a fair profit. Another evil effect of cut-throat competition is the tendency for producers to manufacture to meet a price rather than to maintain quality."

The concluding comments are given in full:

"And finally, and perhaps most important for the public welfare, the effect of this bill would be to put the small local dealers more nearly on a competitive basis with the great chain store and other combinations. It is generally and properly recognized that the gradual extinction of small independent dealers will be a loss to countless communities throughout the Nation, and so to the Nation itself. A small independent dealer who is identified with the community where his store exists, and who is active in its life as a citizen and taxpayer, is surely more advantageous to that community than a mere selling agency of a foreign concern, which agency has no interest in the community except to make what profit it can from the community.

"For the reasons set forth, therefore, the committee believe that the legislation proposed in the bill will be to the public interest, and recommend its passage."

Thanks are due to Congressman Kelly and his supporters for their continued and persistent efforts. The interest of individuals and organizations should not wane but be continued until the bill has become law and, thereafter, they should see that the law is made effective.

H. R. 9053 AND H. R. 9054.

The former Porter Bill is represented by the two bills now before Congress—the first seeks to create a Bureau of Narcotics and the other recites as its purpose "to further carry into effect the international convention for the suppression of the abuse of opium and other drugs signed at The Hague on January 23, 1912, and for other purposes." The bills follow, and elsewhere are printed the viewpoints of pharmacists who discussed the subject with Congressman Porter.

H. R. 9053.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That there shall be in the Department of the Treasury a bureau to be known as the Bureau of Narcotics and a Commissioner of Narcotics who shall be at the head thereof. The Commissioner of Narcotics shall be appointed by the Secretary of the Treasury, without regard to the civil service laws, and shall receive a salary at the rate of $9000 per annum. The commissioner shall make an annual report to Congress.

SEC. 2. (*a*) The Secretary of the Treasury may, without regard to the civil service laws, appoint one assistant commissioner, and subject to the provisions of the civil service laws and in accordance with the Classification Act of 1923, as amended, appoint and fix the compensation of two deputy commissioners, and such other officers and employees as, in the judgment of such Secretary, are necessary to execute the functions vested in such bureau.

(*b*) In order to aid in the detection and prevention of the unlawful importation of narcotic drugs into the United States, the Commissioner of Narcotics may designate certain officers of the Bureau of Narcotics for assignment to duty at ports of entry or other places specified by such commissioner. Such officers shall, during the period of such assignment and at such ports and places, have the same power and authority as customs officers have in the enforcement of the narcotic drug laws of the United States.

SEC. 3. (*a*) The Federal Narcotics Control Board established by the Narcotic Drugs Import and Export Act, as amended, is hereby abolished, and all the authority, powers and functions exercised by such board are hereby transferred to and shall be vested in and exercised and performed by the Commissioner of Narcotics. The Surgeon General of the Public Health Service shall designate three medical officers of the Public Health Service to investigate and report to the commissioner not later than the 1st day of September each year as to the amounts of crude opium and coca leaves necessary to supply the medicinal and scientific needs of the United States for the following calendar year. Such report shall be given due consideration by the Commissioner of Narcotics in finding the amounts of crude opium and coca leaves to be imported under such Act, as amended.

(*b*) All rights, privileges, powers and duties conferred or imposed upon the Commissioner of Prohibition or any officer or employee of the Bureau of Prohibition in respect of the taxation, importation, exportation, transportation, manufacture, production, compounding, sale, exchange, dispensing, giving away or possession of narcotic drugs are hereby transferred to, conferred and imposed upon, the Commissioner of Narcotics.

(*c*) All the officers and employees in the Bureau of Prohibition who are exclusively engaged, on the date this Act takes effect, in the administration or enforcement of any laws relating to narcotic drugs, except the Commissioner of Prohibition, are hereby transferred to the Bureau of Narcotics without change in classification or compensation.

(*d*) All the official records, papers and property (including furniture and office equipment) in the Bureau of Prohibition pertaining to or in use in the administration or enforcement of any narcotic drug laws are hereby transferred to the Bureau of Narcotics.

(*e*) All unexpended balances of appropriations under the control of the Bureau of Prohibition for the enforcement of any laws relating to narcotic drugs and available on the date this Act takes effect shall be available for expenditure by the Bureau of Narcotics in the same manner and to the same extent as if the Bureau of Narcotics had been directly named in the laws making such appropriations.

(*f*) All orders, rules and regulations in respect of any laws relating to narcotic drugs which have been issued by the Commissioner of Prohibition and the Federal Narcotics Control Board and which are in effect on the date this Act takes effect shall, after such date, continue in effect to the same extent as if the transfer had not occurred, until modified, superseded or repealed by the Commissioner of Narcotics.

(*g*) All proceedings, investigations and other matters pending in or before the Bureau of Prohibition and the Federal Narcotics Control Board in respect of the administration or enforcement of any laws relating to narcotic drugs shall be continued and brought to final determination before the Bureau of Narcotics.

SEC. 4. This Act shall take effect sixty days after the date of its enactment.

H. R. 9054.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That (*a*) in order to more effectively carry out the provisions of the international convention for the suppression of the abuse of opium and other drugs signed at The Hague on January 23, 1912, the Commissioner of Prohibition shall, with the approval of the Secretary of the Treasury, prescribe such rules and regulations as may be necessary for the issuance and for the suspension and revocation of licenses as hereinafter provided.

(*b*) It shall be unlawful for any person to import, manufacture, produce, compound, sell, deal in, dispense or give away any narcotic drug unless such person has in his possession a valid license issued by the Commissioner of Prohibition to such person as provided in this Act. Such license shall set forth the nature of the business or profession to be carried on, the applicant's name or style, place of business or profession, and such other matters as the commissioner may by regulation prescribe. No license shall be issued, or if issued such license may be suspended or revoked, if it is shown to the satisfaction of the commissioner that (1) the applicant or licensee is a narcotic drug addict, or (2) the applicant or licensee has been convicted of violating the law of any State or of the United States relating to narcotic drugs. No license for the importation or manufacture of any narcotic drug shall be issued, or if issued such license may be suspended or revoked, if the commissioner finds that such license is not necessary to supply the medicinal and scientific needs of the United States.

(*c*) Prior to the issuance, suspension or revocation of a license under this section, the Commissioner of Prohibition may give written notice to the applicant or licensee to show cause why the license should be issued, or in case a license has been issued, why such license should not be suspended, or revoked, as the case may be. Within twenty days after such notice is received the applicant or holder may file a written request with the Commissioner of Prohibition for a hearing, together with the reasons why the application should be issued or the license should not be suspended or revoked. The commissioner, upon the receipt of the request, shall forthwith (1) arrange for a hearing to be held within twenty days after such receipt at such place as the commissioner deems most practicable and convenient in view of the place of residence of the applicant or holder and the place where the evidence bearing on the case for the proposed denial, suspension or revocation is most readily obtainable, and (2) give the applicant or holder at least ten days' notice of the hearing, unless an earlier hearing is consented to by him. Notice under this subdivision may be served personally upon the applicant or holder or sent him by registered mail. The commissioner, or any officer or employee of the Bureau of Prohibition designated by him in writing for the purpose, may hold any such hearing and for the purposes thereof administer oaths, examine witnesses, and issue subpœnas for the attendance and testimony of the witnesses, or the production of books, papers, documents and other evidence, or the taking of depositions before any designated individual competent to administer oaths. Upon request of the applicant or licensee the person holding such hearing shall issue such subpœnas as in his judgment are necessary in the prosecution of the hearing. Witnesses summoned or whose depositions are taken shall receive the same fees and mileage as witnesses in courts of the United States. All evidence taken at the hearing shall be recorded and forwarded to the commissioner for decision in the matter to be rendered by him not later than thirty days after completion of the hearing. The denial, suspension or revocation of the license shall be invalid unless opportunity for hearing is afforded, notice is served or sent, and decision rendered within the respective time prescribed by this sub-division.

(*d*) Any person whose application for a license has been denied or whose license has been suspended or revoked, as hereinbefore provided for, may appeal from the decision of the commissioner to the Supreme Court of the District of Columbia or to the district court of the United States in which is located the principal place of business of such applicant or licensee, by filing with such court notice in writing of such appeal and of the reasons therefor.

(*e*) Any person who violates the provisions of this section shall be guilty of an offense punishable by fine not exceeding $5000 or imprisonment not exceeding two years, or by both such fine and imprisonment.

(*f*) As used in this section, the term "narcotic drug" means opium or coca leaves, or any compound, manufacture, salt, derivative or preparation thereof, except preparations of coca leaves which do not contain cocaine or ecgonine.

(*g*) As used in this section, the term "person" means corporation, association or partnership, as well as an individual.

SEC. 2. If any provision of this Act is declared unconstitutional, or the applicability thereof to any person, circumstance or narcotic drug is held invalid, the validity of the remainder of the Act and the applicability of such provision to other persons, circumstances or narcotic drugs shall not be affected thereby.

SEC. 3. This Act shall take effect six months after the date of its enactment.

BOOK NOTICES AND REVIEWS.

Die Methoden der Organischen Chemie. Unter Mitarbeit von Autoritäten herausgegeben von PROF. DR. J. HOUBEN, Berlin 3. Auflage III. Band mit 41 Abbildungen. Octavo, 1451 pages, gebunden 176 M. Georg Thieme Verlag, Antonstr. 15 Leipzig. C. 1.

Each chapter in this masterwork is prepared by an authority in the respective subject. The one on Tannins, occupying pages 961 to 1009 is by Dr. J. Dekker in The Hague, well known for his researches. The chapter on Carbohydrates pp. 228 to 365 is by such authorities as Prof. Dr. Hans Pringsheim and Dr. Arnold Steingroever in Berlin.

As a proof of the thoroughness of the work, let me quote the subdivision of the chapter

on Organic Sulphur Compounds: 1, General; 2, Mercaptanes; 3, Sulphides or Thio-ethers; 4, Sulphonium Compounds; 5, Disulphides; 6, Sulphoxides and Sulphones; 7, Sulphone Acids and Derivatives; 8, Sulphine Acids; 9, Sulphine Acids and Their Chlorides; 10, Thionylamines; 11, Thio- and Dithiocarbonic Acids; 12, Thio Derivatives of Carbonic Acid; 13, Thio Aldehydes and Thio Ketones.

The chapter on Aldehydes and Ketones prepared by such an authority as Prof. Dr. Julius Schmidt in Stuttgart, concludes with a very convenient and complete table of Reagents for these substances, occupying three pages.

The chapter on Halogen Compounds, pages 1060–1229, with 8 illustrations, is divided into 3 parts: I. Halogenation (Fluorination, Chlorination, Bromination and Iodination); II. Qualitative and Quantitative Determination of Organic Halogen; and III. Dehalogenation. The chapter concludes with General Methods of Preparation and Reactions of Organic Halogen Compounds.—OTTO RAUBENHEIMER.

Mercks Index. Fourth Edition. An encyclopedia for the chemist, pharmacist and physician, giving the names and synonyms; source, origin or mode of manufacture; chemical formulas and molecular weights; physical characteristics; melting and boiling points; solubilities; specific gravities; medical action; therapeutic uses; ordinary and maximum doses; incompatibilities; antidotes; special cautions; hints on keeping and handling, etc., of the chemicals and drugs used in chemistry, medicine and the arts together with an appendix containing: Reactions of the more important alkaloids and glucosides; characteristic reactions of acids, bases, metals and salts; table of atomic weights; thermometric equivalents; specific gravity tables; metric conversion tables; and abbreviations. 600 pages, $6^1/_2$ x $9^1/_2$". Publishers, Merck & Co., Rahway, N. J. Price, $5.00—a 50 per cent reduction will be made to members and those affiliated with the pharmaceutical, chemical, medical and allied professions; *i. e.*, a net price of $2.50.

The fourth edition of the American series of *Merck's Index* will be welcomed by pharmacists; supplementary tables and tests have been added to the edition of 1907. The information contained in this encyclopedia represents the work of many and, excepting the standards, there are few other books that have greater usefulness for the pharmacist. While those who have been engaged in pharmacy for a decade or two are familiar with the *Index*, those who have entered the profession in more recent years should become acquainted with it, because of its usefulness as a reference book. The monographs are comprehensive, but in condensed form; the list of the introductory paragraph gives a general idea of the contents of the *Index*.

Posology, Percentages, Poisons. By JOHN CAMERON, Ph.C., F. C. S.; pharmacist Peking Union Medical College. The author is a member of the AMERICAN PHARMACEUTICAL ASSOCIATION. The tables have been taken from the British Pharmacopœia and grouped for the convenience of pharmacy students in China; students are examined on these doses in their posology examinations for the dispenser's certificate and pharmacists diploma of the North China Pharmaceutical Society. The booklet also contains percentage tables, equivalents in weights and measures, incompatibilities and abbreviations used in prescription writing. Several of the abbreviations are confusing: L. for lac; Mr. for Mistura. We are wondering why an abbreviation Z. Z. for Zingiber should be necessary; no other abbreviation for a vegetable drug is given. These are merely incidental comments; the booklet doubtless serves the intended purpose; we hereby make grateful acknowledgment of the copy sent us.

The Reagents and Reactions of Deutschen Arzneibuch, VI. A Chemistry and Criticism and History, by DR. HERBERT HARMS, Published by the den Deutschen Apotheker Verein. Price, Rm. 15.

REVIEWS OF THE PHARMACEUTICAL RECIPE BOOK.

Nearly all of the foreign pharmaceutical publications have reviewed "The Pharmaceutical Recipe Book"and it is understood that all of the United States publications have done so. A general expression of thanks for the courtesy is due them and gladly extended. The reviews have been quite favorable and nearly all of the publications have made one or more suggestions which will help the Committee in the preparation of the next edition.

Other reviews have been held over on account of matter in other Sections.